Core temperature is a critical vital sign that should be monitored throughout the perioperative journey.

<table>
<thead>
<tr>
<th>Method</th>
<th>Invasive</th>
<th>Accuracy</th>
<th>Anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>3M™ Bair Hugger™ Temperature Monitoring System</td>
<td>No</td>
<td>High</td>
<td>☑ ☑ ☑</td>
</tr>
<tr>
<td>Pulmonary Artery</td>
<td>Yes</td>
<td>High</td>
<td>☑</td>
</tr>
<tr>
<td>Esophageal</td>
<td>Yes</td>
<td>Medium/High</td>
<td>☑</td>
</tr>
<tr>
<td>Nasopharyngeal</td>
<td>Yes</td>
<td>Medium/High</td>
<td>☑</td>
</tr>
<tr>
<td>Oral</td>
<td>No</td>
<td>Medium</td>
<td>☑</td>
</tr>
<tr>
<td>Bladder</td>
<td>Yes</td>
<td>Medium</td>
<td>☑ ☑ ☑</td>
</tr>
<tr>
<td>Skin</td>
<td>No</td>
<td>Lowest</td>
<td>☑ ☑ ☑ ☑</td>
</tr>
</tbody>
</table>

- General Anesthesia
- Mac/Regional
- No sedation

More to be done for the older patients

Anesthesia for the patient with a recently diagnosed concussion: think about the brain!

Anesthetic management of geriatric patients

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Anesthesia for the patient with a recently diagnosed concussion: think about the brain!

Mohammed R. Rasouli, Michelle Kavin, Stephen Stache, Michael E. Mahla, Eric S. Schwenk

1Department of Anesthesiology, Duke University School of Medicine, Durham, NC, 2Rothman Orthopedics, Departments of 3Family and Community Medicine, 4Anesthesiology, Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA, USA

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Corresponding author:
Eric S. Schwenk, M.D.
Department of Anesthesiology, Sidney Kimmel Medical College at Thomas Jefferson University, 111 South 11th Street Gibbon Building, Suite 8290 Philadelphia, PA 19107, USA
Tel: +1-215-955-6161
Email: Eric.Schwenk@jefferson.edu
ORCID: https://orcid.org/0000-0003-3464-4149

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Anesthetic management of geriatric patients

Byung-Gun Lim, Il-Ok Lee

Department of Anesthesiology and Pain Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, Korea

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Preoperative risk factors for massive transfusion, prolonged ventilation requirements, and mortality in patients undergoing liver transplantation

간이식을 받는 환자의 대량 수혈과, 기계적 인공호흡, 사망률과 관련된 수술 전 위험 인자

Dennis Danforth¹, Rodney A. Gabriel¹², Anthony J. Clark¹, Beverly Newhouse¹, Swapnil Khoche¹, Sanjana Vig¹, Ramon Sanchez¹, Ulrich H. Schmidt¹

Departments of ¹Anesthesiology, ²Biomedical Informatics, University of California San Diego, La Jolla, CA, USA

배경: 간이식의 술기와 환자 관리의 발전에도 불구하고, 수술 전후의 사망률을 높이는 합병증 문제는 여전히 남아있다. 간이식을 받는 환자에게 수술 중에 대량 수혈이 필요할 것인지, 기계적 인공호흡이 얼마나 오래 필요한지, 환자의 병원 내 사망률이 얼마나 될 것인지 예측할 수 있는 기준은 아직 밝혀지지 않았다. 본 연구에서는 상기 언급된 합병증과 관련된 수술 전 인자를 밝히고자 한다.

방법: 2014년부터 2017년 사이에 단일 기관에서 시행한 124건의 정규 간이식 사례들을 후향 관찰 분석하였다. 수술 전 특성과 대량 수혈, 장기간의 기계적 인공호흡, 사망률의 연관 관계를 밝혀내기 위해 다변량 로지스틱 회귀법을 사용하였다. 10백 이상의 농축 적혈구를 사용했을 때 대량 수혈이라고 정의하며, 기계적 인공호흡을 한 시간이 24시간을 초과할 때 장기간 기계적 인공호흡이라고 정의한다.

결과: 대량 수혈과 유의한 연관 관계가 있는 인자는 간세포암과 수술 전 농축적혈구 수혈이었 다. 장기간 기계적 인공호흡과 유의한 연관 관계가 있는 인자는 C형 간염, 알코올성 간염, 수술 전 상승된 ALT, 간신중후군이었다. 남성의 경우 장기간의 기계적 인공호흡이 덜 필요하였다. 발기 심장 질환과 B형 간염은 병원 내 사망률과 유의하게 관련이 있었다.

결론: 본 연구는 간이식의 일반적인 수술 전후 합병증의 위험 인자를 밝혀내었다. 이러한 인자를 알아두면 의사가 환자의 위험도를 분류할 때 도움이 될 수 있으며, 향후 이러한 위험을 완화할 수 있는 의료적 개입 방법 연구를 위한 기반이 되어줄 수 있다.

Keywords: Artificial respiration; Blood transfusion; Hepatitis C; Hepatocellular carcinoma; Liver cirrhosis; Liver transplantation.
Effect of anesthetic method on incidence of delirium after total hip replacement arthroplasty in South Korea: a population-based study using National Health Insurance claims data

Eun-Ji Choi¹, Yoon Ji Choi², Sang Won Lee², Yun-Mi Choi¹, Hyun-Su Ri¹, Ju Yeon Park¹, Soon Ji Park¹, Jung-Min Son³, Yoon Sook Lee²

¹Department of Anesthesia and Pain Medicine, Pusan National University Yangsan Hospital, Yangsan, ²Department of Anesthesiology and Pain Medicine, Ansan Hospital, Korea University College of Medicine, Ansan, ³Department of Biostatistics, Clinical Trial Center, Biomedical Research Institute, Pusan National University Hospital, Busan, Korea

Keywords: Delirium; General anesthesia; Korean National Health Insurance claims data; Regional anesthesia; Total hip replacement arthroplasty.

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Corresponding author:
Yoon Ji Choi, M.D., Ph.D.
Department of Anesthesiology and Pain Medicine, Korea University Ansan Hospital, 123 Jeokgeum-ro, Danwon-gu, Ansan 15355, Korea
Tel: +82-31-412-5297
Fax: +82-31-412-5294
Email: yoonji07@gmail.com
ORCID: https://orcid.org/0000-0003-3031-357X

배경: 고관절 수술의 마취 방법 선택에 따라 신경학적 합병증에 가까운 영향에 관한 다양한 결과가 보고되고 있다. 이에 본 연구는 국민건강보험 청구자료를 이용하여 마취 방법이 국내의 고관절 전치환술 후 섬망 발생빈도에 미치는 영향을 분석하기 위한 연구를 진행하였다.

방법: 국민건강보험 청구기록을 사용하여 2008년 1월부터 2017년 12월까지 'N0711' 운영코드가 붙은 24,379건의 고관절 전치환술 사례를 후향적으로 추출하였다. 마취 청구코드에 따라 환자를 9,921건의 전신마취 그룹과 14,458건의 부위마취 그룹, 두 그룹으로 나누었다. 환자들이 할로페리돌(haloperidol), 클로르프로마진(chlorpromazine), 올란자핀(olanzapine), 리스페리돈(risperidone)과 같이 섬망에 쓰이는 약을 복용한 사례들을 사용하여 섬망의 발생빈도를 평가하였다.

결과: 전신마취를 받은 9,921명의 환자와 부위마취를 받은 14,458명의 환자 중, 각각 142명(1.43%)과 209명(0.86%)이 고관절 전치환수술 후 섬망을 경험하였다. 두 그룹 간의 유의한 차이는 없었다(\(P = 0.92\)). 그리고 로지스틱 회귀 분석법을 사용하여, 환자의 성별(\(P = 0.038\))과 후천적 면역결핍증후군의 유무(\(P = 0.008\))가 수술 후 섬망 발생의 예측 인자임을 발견하였다.

결론: 본 연구의 결과에 따르면 고관절 수술 환자에서 마취 방법과 수술 후 섬망 발생은 서로 연관이 없었다. 그리고 남성 환자와 후천적 면역결핍증후군을 가진 환자는 고관절 전치환수술시 시행하는 경우, 수술 후 섬망이 일어나지 않도록 주의가 필요하다.
Ultrasound-guided anterior quadratus lumborum block for postoperative pain after percutaneous nephrolithotomy: a randomized controlled trial

Korgün Ökmen1, Burcu Metin Ökmen2

Departments of 1Anesthesiology and Reanimation, 2Physical Medicine and Rehabilitation, University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital, Yildirim, Bursa, Turkey

배경: 복부 통증완화 치료법으로 알려진 전방 요방형근 차단술은 새로이 보고된 근막층면 차단술이다. 본 연구의 목표는 초음파 유도하의 전방 요방형근 차단술이 경피적 신절석술 후의 통증 정도에 어떤 효과가 있는지 조사하는 것이다.

방법: 본 실험은 전향적 무작위 대조 단순 맹검법으로 이루어졌으며, 경피적 신절석술을 받은 60명의 환자를 무작위로 두 그룹에 배정했다. B 그룹(30명)은 전방 요방형근 차단술과 정맥 자가 통증조절법을 병용하였고, C 그룹(30명)에는 차단술 없이 정맥 자가 통증조절법만을 시행하였다. 수술 후 24시간 동안 VAS를 이용한 통증점수 및 모르핀 소모량을 측정하였고, 부가적으로 부작용, 수술 후 추가 진통제 요구량, 수술 중 마약성 진통제 소모량을 기록하였다.

결과: B그룹에서 수술 후 6시간, 12시간, 24시간에 사용된 모르핀의 평균값이 통계적으로 유의하게 낮은 것으로 나타났다(P < 0.05). VAS를 이용한 통증점수 또한 B그룹에서 통계적으로 유의하게 낮았다(P < 0.05). 부작용, 추가 진통제 요구량, 수술 중 마약성 진통제 소모량은 그룹간에 통계적으로 유의한 차이가 없었다(P > 0.05).

결론: 본 연구 결과는 전방 요방형근 차단술이 경피적 신절석술 후 통증 완화를 위한 효과적인 치료 방법임을 제시한다.

Keywords: Fascia; Local anesthetic; Pain; Percutaneous nephrolithotomy; Quadratus lumborum block; Ultrasonography.
이동수단이 소아 환자의 수술 전 불안감에 끼치는 영향: 무작위 대조 실험

Sun-Hong Park, Sanghee Park, Seongheon Lee, Jeong Il Choi, Hong-Beom Bae, Youngwook You, Seongtae Jeong

Department of Anesthesiology and Pain Medicine, Chonnam National University Medical School and Hospital, Gwangju, Korea

배경: 본 연구는 수술실 내 이동 방법으로 일반적인 환자 운반카(stretcher car)보다 소아가 좋아할 만한 작은 유아용 자동차(wagon)를 이동수단으로 사용했을 때 소아 환자가 부모와 떨어졌을 때의 불안감을 줄일 수 있는지 평가하기 위해 수행되었다. 이차적인 목표는 이러한 불안감이 나이와 연관관계가 있는지 평가하는 것이다.

방법: 정규수술을 받는 2-7세의 80명의 소아 환자를 두 그룹으로 무작위 배정하였다. Stretcher군은 일반적인 환자 운반카로 수술실까지 이동하였으며, Wagon군은 유아용 자동차로 수술실까지 이동하였다. 소아의 불안 정도는 modified Yale Preoperative Anxiety Scale (mYPAS)을 사용하여, 대기실(T0), 수술실 이동 중 복도(T1), 전신마취 유도 직전(T2), 불안 수준을 세 번 측정하였다.

결과: 수술실 이동 중(T1) 환자의 불안 수준은 Wagon군(36.7 [31.7, 51.7])이 Stretcher군(51.7 [36.7, 83.3])보다 유의하게 낮았다(P = 0.007). 하지만, 마취유도 직전(T2) 두 그룹 간의 불안 수준 차이가 없었다(각각 46.7 [32.5, 54.2]와 51.7 [36.7, 75.0], P = 0.057). 대기실에서의 불안정도(T0)는 나이가 들수록 낮아지는 경향을 보였다(r = -0.248, P = 0.031). Stretcher군에서 나이가 들수록 수술실로 이동하는 동안 불안 수준의 증가도가 높았다(r = -0.340, P = 0.034). 그러나 wagon군에서는 어떠한 상관관계도 관찰되지 않았다(r = -0.053, P = 0.756).

결론: Wagon을 이용하여 수술실까지 이동하는 방법으로 소아 환자의 불안감을 줄일 수 있으며, 이 방법은 수술 전 소아 환자의 불안 수준을 낮추는 좋은 대안이 될 수 있다.

Keywords: Anxiety; Child; Operating rooms; Separation; Stretchers; Transportation of patients.
The effect of the type of anesthesia on the quality of postoperative recovery after orthopedic forearm surgery

정형외과 전완부 수술을 받는 환자에서 마취 방법이 수술 후 회복의 질에 미치는 영향

A Ram Doo¹,², Sehrin Kang¹, Ye Sull Kim¹, Tae-Won Lee¹, Jun-Rae Lee¹,², Dong-Chan Kim¹,²

¹Department of Anesthesiology and Pain Medicine, Jeonbuk National University Hospital,
²Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, Jeonju, Korea

배경: 수술 후 회복의 과정에서 여러 요인이 영향을 미칠 수 있지만, 마취 방법이 마취의 영향에 대한 연구는 부족한 실정이다. 이 연구는 단일맹검 전향적 관찰연구로서, 전신 또는 부위마취(상완신경총차단술) 하에 정형외과 전완부 수술을 받는 환자를 대상으로 마취 방법에 따른 수술 후 회복의 질을 비교하였다.

방법: 정형외과 전완부 수술이 예정된 미국마취과학회 신체상태 분류(ASA PS) I 또는 II에 해당하는 18–65세 환자 97명을 전신마취 또는 부위마취 집단에 배정하였다. 수술 후 환자의 QoR-40 설문(QoR-40K)을 이용하여 평가하였다. 전신마취 전기저치, 수술 후 1일차 및 7일차에 총 3번을 조사하였으며, 두 집단의 점수를 비교하였다.

결과: 전신 마취는 47명, 부위 마취는 50명의 환자의 데이터를 분석하였다. 전체적 QoR-40K 점수 및 5개 차원 각각에서 두 집단은 기저치, 수술 후 1일차 및 7일차에 유의한 차이를 보이지 않았다. 이원 RM ANOVA에서 두 집단 모두 수술 후 1일차의 전반적 QoR-40K 점수는 기저지(P < 0.001) 및 수술 후 7일차(P < 0.001)보다 유의하게 낮았다. 하지만 각 시점에서 두 집단 사이에는 유의한 차이가 없었다.

결론: 본 연구는 정형외과 전완부 수술을 받는 환자에서 레미펜타닐(remifentanil) 지속주입 및 세보플루(sevoflurane)로 환기마취와 비교하여 상완신경총차단질 및 테스메데토미딘(dexmedetomidine) 정맥주입을 통한 진정이 수술 후 회복의 질을 개선하지 않는다는 점을 제시하였다.

Keywords: General anesthesia; General surgery; Orthopedic surgery; Postoperative recovery; Quality; Regional anesthesia.
Combined supraclavicular and superficial cervical plexus block for clavicle surgery

Onur Baran¹, Bünyamin Kir¹, İrem Ateş¹, Ayhan Şahin², Ali Üztürk³

¹Clinic of Anesthesiology and Reanimation, Palandöken State Hospital, Erzurum, ²Department of Anesthesiology and Reanimation, Medical Faculty of Namik Kemal University, Tekirdağ, ³Clinic of Orthopedics and Traumatology, Palandöken State Hospital, Erzurum, Turkey

Keywords: Clavicle; Nerve block; Ultrasonography.
Sudden hemodynamic collapse after prone positioning on a Jackson spinal table for spinal surgery

Jae Hong Park, Ji Yeon Kwon, Sang Eun Lee, Yong Han Kim, Se Hun Kim

Department of Anesthesiology and Pain Medicine, Haeundae Paik Hospital, Inje University College of Medicine, Busan, Korea

Case Report

Keywords: Circulatory collapse; General anesthesia; Obesity; Prone; Spinal stenosis; Systemic hypotension.

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Corresponding author:
Se Hun Kim, M.D.
Department of Anesthesiology and Pain Medicine, Haeundae Paik Hospital, Inje University College of Medicine, 875 Haeundae-ro, Haeundae-gu, Busan 48108, Korea
Tel: +82-51-797-0478
Fax: +82-51-797-0499
Email: anesehunkim@gmail.com
ORCID: https://orcid.org/0000-0002-2752-2883

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Cognitive recovery after anesthesia and surgery is a concern for older adults, their families, and caregivers.

In the recent years, an increasing number of older adults have been undergoing anesthesia and surgery. In the western countries, approximately 37% of all surgical procedures were performed on patients more than 65 years of age in 2010, accounting for more than 19 million patients in the USA [1].

In this current issue of the Korean Journal of Anesthesiology, Choi et al. [2] reported that anesthetic methods were not associated with the incidence of postoperative delirium through a retrospective analysis of the Korean National Health Insurance claims database including 24,379 cases of total hip replacement arthroplasty. In their report, the incidences of 1.43% and 0.86% in the general and regional anesthesia groups, respectively, were substantially lower than those reported in other studies [3–5]. This discrepancy may be a result of the differences in methods of diagnosing delirium. Choi et al. identified postoperative delirium as the use of postoperative medication for delirium, such as haloperidol, chlorpromazine, olanzapine, and risperidone, as it was not possible to diagnose delirium using the Mini-Mental State Examination or Confusion Assessment Method. Therefore, the incidence of mild or hypoactive delirium may have been overlooked and, consequently, the incidence of postoperative delirium underestimated.

An early diagnosis of postoperative delirium (POD) is critical for a focused and effective treatment [6–11]. The latest clinical guidelines by European Society of Anaesthesiology recommend that patients should not leave the recovery room without being screened for POD [12]. If POD is detected, patients should not be discharged from the recovery room to the ward without having started an etiology- and symptom-based treatment [13]. This is for cases of delirium with a longer duration, and with delayed treatment, cognitive decline may be expected [14]. At the postoperative ward, POD should be monitored at least once per shift because of the fluctuating course of POD [12,15].

In this study by Choi et al. [2], diagnoses of hyperactive delirium were disproportionately represented in comparison with the hypoactive type. Hypoactive delirium is more common than hyperactive delirium [16–18], however, recent retrospective studies found notably lower incidence of hypoactive delirium because of the possible lack of routine screening for symptoms delirium [2,5,19]. For this reason, hypoactive delirium is detected late in time and has the worst prognosis.

The authors concluded that anesthetic methods are not associated with the incidence of postoperative delirium; therefore, depending on the patient's condition and the anesthesiologist's experience, both anesthetic methods should be considered in total hip replacement arthroplasty. However, many older patients and caregivers suffer from POD and its subsequent adverse events.

More rigorously designed multicenter randomized clinical trials and large-scale observational studies are required to determine which is the most appropriate anesthetic tech-
nique, and whether the current best practice recommendations, such as the preoperative cognitive function assessment and routine screening of POD, reduce the incidence of all forms of POD.

References


Some patients require emergent, urgent, or elective surgery in the time period immediately following diagnosis of concussion. However, changes in brain homeostatic mechanisms following a concussion and concern for secondary brain injury can complicate the decision as to whether or not a surgery should proceed or be postponed. Given the paucity of available evidence, further evaluation of the use of anesthesia in a patient with concussion is warranted. This article summarizes what is currently known about the relevant pathophysiology of concussion, intraoperative anesthesia considerations, and effects of anesthesia on concussion outcomes in an attempt to help providers understand the risks that may accompany surgery and anesthesia in this patient population. While most contraindications to the use of anesthesia in concussed patients are relative, there are nonetheless pathophysiologic changes associated with a concussion that can increase risk of its use. Understanding these changes and anesthetic implications can help providers optimize outcomes in this patient population.

Keywords: Brain concussion; Brain ischemia; General anesthesia; Intracranial hypotension; Post-concussion syndrome.

Introduction

According to the American Medical Society for Sports Medicine’s position statement, concussion is defined as a traumatically induced transient disturbance of brain function involving a complex pathophysiological process [1]. It has been estimated that as many as 3.8 million sports-related concussions occur annually. However, data suggest that up to 50% of concussions go unreported and the actual occurrence rate is much higher [2]. The majority of patients with concussions (80% to 90%) recover within seven to 10 days after the injury [3]; however, some patients develop persistent post-concussion symptoms and can need more than four weeks to recover [4-6].

During this time period when a patient is recovering from a concussion, patients with a recent concussion will sometimes require surgery that may or may not be related to the head injury [7]. In some cases, providers will need to counsel patients on which procedures need to be completed promptly and which need to be postponed until the concussion symptoms resolve. This decision is complicated because changes in brain physiology and concern for secondary exacerbation of functional neurological dysfunction can make administration of anesthesia more challenging [8] and few studies have been performed evaluating the impact anesthesia has on concussion symptoms [7,9].

Since there are no current clinical guidelines to rely on in these situations, clinical
judgment must be used to decide when the risks of postponing the surgery outweigh the possible risks of anesthesia to a patient with a diagnosis of concussion. Therefore, in order to help providers understand the risks of anesthesia as it relates to concussion, this review will summarize what is currently known about the relevant pathophysiology of concussion, intraoperative anesthesia considerations, and effects of anesthesia on concussion outcomes.

**Pathophysiology of concussion**

After an acceleration/deceleration injury, complex pathophysiologic changes in the brain occur including ionic shifts, changes to cerebral blood flow (CBF) autoregulation, alterations in cerebral metabolism, release of neurotransmitters, changes to the blood-brain barrier integrity, and expression of inflammatory cytokines (Table 1) [7]. While a full discussion of all changes is beyond the scope of this article, ionic shifts, altered CBF autoregulation, and autonomic nervous system dysfunction warrant review.

Concussions are associated with ionic shifts. Studies have shown that following brain injury, an ionic shift occurs at a cellular level, altering the neuronal transmembrane potential [10]. Restoration of a normal neuronal transmembrane potential requires an increase in activity of sodium-potassium (Na⁺-K⁺) pumps. In turn, glucose metabolism must increase to meet the needs of the sodium-potassium pumps. When glucose supply cannot match this demand, anaerobic metabolism occurs leading to an accumulation of intracellular lactate. As a short-term solution, an increase in intracellular calcium and sequestration of calcium into mitochondria occurs. However, calcium sequestration can eventually lead to mitochondrial dysfunction, impair mitochondrial oxidative metabolism, and worsen the energy deficit activating pathways that lead to cell death [9]. These changes create a vulnerable state that can potentially be complicated by the stresses of surgery and anesthesia.

In addition to the neuronal metabolic changes, a severity-dependent decrease in CBF occurs following concussion [11-14]. This injury-induced decrease in CBF further worsens the imbalance between oxygen demand and supply. The decrease in CBF and perfusion deficit following sport-related concussions can last for a month or longer prolonging recovery and increasing the duration of measurable symptoms [15].

In order to understand the significance of this change, it helps to review normal CBF autoregulation. In the normal brain, several homeostatic mechanisms assist in coupling cerebral oxygen demand with oxygen supply. The most important of these mechanisms include pressure autoregulation, CBF changes in response to a change in arterial partial pressure of carbon dioxide (PaCO₂), and CBF changes in response to metabolic demand. Changes in arterial PaCO₂ induce a pH difference between the blood and the cerebrospinal fluid, which through several proposed mechanisms results in a linear direct relationship between PaCO₂ and CBF. Changes in arterial PaCO₂ of 20 and 60 torr. Increased PaCO₂ results in arterial dilation and blood flow to the brain increases approximately 2 cc/100 g/min per torr increase. Conversely, decreasing PaCO₂ will result in a similar decrease in CBF [16].

Following minor traumatic brain injury, efficacy of pressure autoregulation is reduced [14] and CBF becomes more linearly related to mean arterial pressure whereas the response to changes in PaCO₂ remains relatively intact. Therefore, given the reduced capabilities of pressure autoregulation, the combination of hyperventilation and even mild hypotension can lead to significant cerebral ischemia in a patient with concussion, making the use of anesthesia a concern in this patient population.

Autonomic nervous system dysfunction after a concussion may also impact surgical considerations. Dysregulation of the autonomic nervous system in the first 72 h even after mild traumatic brain injury and concussion has been described [17]. Since the autonomic nervous system is responsible for cardiac function, several investigators have attempted to establish the relationship of cardiac function as a measure of the autonomic nervous system’s dysregulation.

One measurement under assessment is heart rate variability, the change in the interval between each heart beat noted as the R wave to R wave (R to R) interval on electrocardiogram. In a systematic review by Blake et al. [18], nine studies were evaluated and the authors concluded that cardiac autonomic function is altered in patients with concussion. It is important to note, however, that the studies in the review were limited by small sample sizes, methodological heterogeneity, and limited follow-up of subjects. In other research, heart rate variability has been introduced as a promising and useful test to assess and monitor athletes with concussion [19]. Overall, while further research is needed to understand this relationship of cardiac function and autonomic nervous system dysfunction in relation to concussion.

<table>
<thead>
<tr>
<th>Table 1. Pathophysiologic Changes Associated with Concussion</th>
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<td>- Ionic shifts shift</td>
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<tr>
<td>- Impaired cerebral blood flow autoregulation</td>
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<td>- Changes to cerebral metabolism</td>
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<td>- Neurotransmitter release</td>
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<td>- Disruption of blood-brain barrier</td>
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<td>- Expression of inflammatory cytokines</td>
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<td>- Autonomic nervous system dysfunction</td>
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it must be recognized that the autonomic nervous system dysfunction may also present a challenge in patients undergoing surgery.

Much remains unknown regarding post-concussion pathophysiology, but the above changes including ionic shifts, altered CBF autoregulation, and autonomic nervous system dysfunction may present challenges for patients requiring anesthesia and surgery. It has also been suggested that a second insult to the concussed brain especially prior to recovery from the first insult, can result in worsened cellular metabolic changes and more significant cognitive deficits [20]. Therefore, it is important to consider the brain's vulnerability after concussion since some of these patients will have concomitant injuries causing hypoxemia, hypotension, anemia, and hyperglycemia that all can worsen the underlying brain injury [1]. An effort should be made to address any concomitant conditions promptly to avoid further brain injury prior to surgical procedures. When patients need to proceed to surgery, it then becomes a matter of how best to ensure optimal outcomes for these patients.

**Intraoperative anesthesia considerations in patients with concussion**

Intraoperative anesthetic management affects hemodynamic, ventilation, and metabolic parameters, and can potentially cause a ‘secondary injury’ to the concussed brain that is vulnerable and already dysfunctional. Because of concern for this secondary injury worsening or prolonging the symptoms of the concussion, it may be prudent to postpone elective surgery until the patient is ready to return to school or normal daily activities [20]. However, some patients need to proceed to the operating room for an urgent or emergent surgery. Therefore, it is useful to discuss intraoperative hemodynamic and metabolic guidelines as well as the effect different routes of administration and types of anesthetic agents may have on this population.

Once the decision has been made to have a procedure, understanding how surgery and anesthetics may interact with the pathophysiologic changes that occur following concussion can help minimize the risk of harm. Since no clear guidelines are available for the subset of patients with concussion, using the intraoperative hemodynamic goals for patients with traumatic brain injury undergoing surgery can serve as a general guide for managing the recently concussed surgical patient (Table 2) [21].

CBF autoregulation is likely impaired [14,22], so even mild hypotension should be avoided to reduce the risk of cerebral hypoperfusion. Maintenance of mean arterial pressure at the patient's baseline value or higher is therefore appropriate. Hypovolemia should be treated using isotonic normal saline rather than hypotonic fluids, which could cause cerebral edema, or colloids, which have been associated with poor outcomes in traumatic brain injury [21]. Since hypocarbia in the face of impaired pressure autoregulation may lead to cerebral ischemia, mechanical ventilation should be adjusted to maintain normocarbia during surgery [21]. Until further research is conducted on the effects of anesthesia on the subset of patients with concussion, utilizing guidelines established for traumatic brain injury may limit risks during procedures.

Current evidence does not provide any guidance regarding choice of anesthetic technique in the patient with concussion. Regional anesthesia, if appropriate for the patient and the surgical procedure, could theoretically hold an advantage in some cases in that it might allow for more hemodynamic stability during certain procedures [23]. However, neuraxial anesthesia can also cause hypotension and few data exist to support this concept.

Considering the effects of individual anesthetic agents can also help defer unintended risk in this patient population. In general, both intravenous and volatile anesthetic agents alter cerebral metabolism and CBF, the two pathophysiologic considerations of importance in patients with concussion. However, no anesthetic drug or technique has been shown to improve outcome in patients with concussion. Therefore, each agent's effects on CBF, metabolism, and response to carbon dioxide must be considered for its relative risks.

Intravenous anesthetic agents generally maintain coupling between cerebral metabolism and CBF. Propofol, one of the most commonly used intravenous sedative-hypnotic medications by anesthesiologists, has been shown to cause cerebral vasoconstriction, reduce CBF, and decrease cerebral metabolic rate for oxygen (CMRO₂) [24]. It is frequently used in patients with recently diagnosed concussion. Ketamine, another intravenous sedative-hypnotic medication, has traditionally been avoided in patients with traumatic brain injury out of concern for increasing CBF and intracranial pressure but a systematic review dispelled that concept [25]. Therefore, as long as an adequate mean arterial pressure is maintained, any of the intravenous anesthetic agents may be used in this patient population.

Volatile anesthetics uncouple CBF and metabolism and result

<table>
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<th>Table 2. Intraoperative Hemodynamic Goals for Patients with Traumatic Brain Injury</th>
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<td>- Avoid hypotension to reduce risk of cerebral hypoperfusion</td>
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<tr>
<td>- Maintain mean arterial pressure at patient's baseline or higher</td>
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<tr>
<td>- Treat hypovolemia with isotonic fluid rather than hypotonic fluid</td>
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<td>- Maintain normocarbia during surgery</td>
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in a dose-dependent decrease in CMRO$_2$ and a simultaneous increase in cerebral blood flow [21]. Like intravenous anesthetic agents, volatile anesthetics can also be used safely in patients with concussion.

In general, while postponing surgeries may be appropriate in some cases, there is no current contraindication for the use of anesthesia in the setting of concussion. When the decision is made to proceed with surgery, steps should be taken to reduce risks associated with a procedure based on understanding the interaction between the pathophysiology of concussion and use of anesthesia during a procedure.

Effects of anesthesia on outcome in patients with concussion

Anesthetic management has the potential to have a significant impact on outcome in concussed patients undergoing surgery. In addition to considering how concussion may affect the use of anesthesia, it is worthwhile to note that there is little information evaluating if anesthesia prolongs the symptoms of concussion. It is possible that the use of anesthesia may create a neurocognitive exacerbation worsening pre-surgical symptoms such as headache, dizziness, postural instability, sleep disturbances, memory impairment, decreased processing speed, attention deficit, fatigue, depression, and anxiety. This concern again suggests that it may be safest to postpone elective surgery until the patient is ready to return to school or normal daily activities if possible [20].

In conclusion, there are multiple pathophysiologic changes in the concussed brain that can make the use of anesthesia for these patients challenging. Unfortunately, without prospective, randomized, controlled trials, the effects of anesthesia on long-term outcomes after concussion remain largely unknown and decisions must be made based on physiologic considerations. The avoidance of hypotension and hypocapnia are prudent and vigilance for the autonomic changes that might occur will help to maximize the chance of a favorable outcome. But given the paucity of currently available information, clinical judgment remains key in decision-making and future studies will be needed to assess the effects between concussion and anesthesia use.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

All authors (Conceptualization; Data acquisition and analysis; Investigation; Methodology; Writing–original draft; Writing–review & editing)

ORCID

Mohammed R. Rasouli, https://orcid.org/0000-0001-7181-5803
Michelle Kavin, https://orcid.org/0000-0002-2968-1693
Stephen Stache, https://orcid.org/0000-0003-0490-7745
Michael E. Mahla, https://orcid.org/0000-0002-7888-6089
Eric S. Schwenk, https://orcid.org/0000-0003-3464-4149

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The number of elderly patients who frequently access health care services is increasing worldwide. While anesthesiologists are developing the expertise to care for these elderly patients, areas of concern remain. We conducted a comprehensive search of major international databases (PubMed, Embase, and Cochrane) and a Korean database (KoreaMed) to review preoperative considerations, intraoperative management, and postoperative problems when anesthetizing elderly patients. Preoperative preparation of elderly patients included functional assessment to identify preexisting cognitive impairment or cardiopulmonary reserve, depression, frailty, nutrition, polypharmacy, and anticoagulation issues. Intraoperative management included anesthetic mode and pharmacology, monitoring, intravenous fluid or transfusion management, lung-protective ventilation, and prevention of hypothermia. Postoperative checklists included perioperative analgesia, postoperative delirium and cognitive dysfunction, and other complications. A higher level of perioperative care was required for older surgical patients, as multiple chronic diseases often makes them prone to developing postoperative complications, including functional decline and loss of independence. Although the guiding evidence remains poor so far, elderly patients have to be provided optimal perioperative care through close interdisciplinary, interprofessional, and cross-sectional collaboration to minimize unwanted postoperative outcomes. Furthermore, along with adequate anesthetic care, well-planned postoperative care should begin immediately after surgery and extend until discharge.

**Keywords:** Aged; Anesthesia; Frail elderly; Geriatrics; Perioperative care.

**Introduction**

The WHO’s ‘World Report on Aging and Health’ revealed significant impairments in the elderly population in Europe, and the number of elderly people is expected to double by 2050 [1]. As the population of a country continues to age, the demands for surgical services increase. Elderly patients often require a higher level of care than younger patients do during the perioperative period, with higher health care costs. Strategies to optimize anesthesia care to reduce complications and improve outcomes in elderly surgical patients will also be of great value to the individual patients and society.

This article reviews the perianesthetic considerations for geriatric patients according to three conceptual categories: preoperative considerations, intraoperative management, and postoperative problems. It also aims to establish a framework to assess the complex issues related to the perioperative care of elderly patients.

The authors performed a comprehensive literature review based on major international databases (PubMed, Embase, Cochrane) and a Korean database (KoreaMed) to identify systematic reviews, meta-analyses, practice guidelines, and clinical trials published in the last 10 years (Appendix 1). The initial search resulted in 1,551 citations and an additional 15 articles were obtained by a manual search through the related references. Of these, the
authors selected 262 publications, which were further narrowed to 172 based on strength of evidence, relevance to geriatric patients, and focused on the perioperative period (Fig. 1).

**Preoperative Management**

**Assessment of functional reserve**

Comprehensive geriatric assessment (CGA) in the preoperative period include systematic evaluation of comorbidities, functional status, neurocognitive function, sensory impairment, substance abuse, frailty, nutrition, and medication. Preoperative CGA has a positive impact on postoperative outcomes in older patients undergoing elective surgery [2]. A recent Cochrane review including 1,583 hip fracture surgeries in subjects ≥ 65 years showed that CGA probably reduces mortality (risk ratio [RR] 0.85, 95% CI 0.68–1.05) and referral to an increased level of care (RR 0.71, 95% CI 0.55–0.92) [2]. However, CGA may make little or no difference in major postoperative complications and delirium rates [3]. Physicians must therefore recommend their patients to undergo all the appropriate preoperative evaluations and interventions such that they can improve their functional reserve and make an informed decision [4,5]. Furthermore, anesthesiologists are strongly encouraged to get involved in national surveys and clinical outcomes research focused on elderly surgical patients [6].

Baseline functional status should first be evaluated in ambulatory patients using a simple screening test, followed by in-depth or full screening of basic and instrumental activities of daily living (ADL) [7,8]. The patient should be evaluated for limitations in gait and mobility using the Time Up and Go (TUG) test [9,10]. In a 2018 prospective cohort study among 131 patients ≥ 65 years old who underwent elective major surgery for cancer, those who were dependent in ADLs and had an unfavorable TUG test had a significantly higher 1-year mortality (odds ratio [OR] 4.5, 95% CI 1.21–18.25, \( P = 0.034 \)) than the other patients. As such, functional assessments such as ADL and TUG test as well as mild cognitive impairment are predictors of long-term outcomes in elderly cancer patients [11]. A 2005 prospective study of 120 patients ≥ 60 years old who underwent thoracic surgery also showed dependence in ADLs and impaired cognitive conditions as important predictors of postoperative complications [12].

Age-associated organ reserve decline, compounded by chronic diseases, also leads to high incidence of postoperative complications in the elderly patient, including neurologic, pulmonary, car-

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**Fig. 1. Flow diagram for article search and study inclusion in this review.**

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Diagnosis and anticipation of common postoperative complications are critical for geriatric surgery. Careful documentation of the patient’s preoperative cognitive status is recommended as a short, easily applicable, and well-studied tool. For patients without a known history of cognitive impairment, “Mini-Cog” is recommended as a short, easily applicable, and well-studied tool. Careful documentation of the patient’s preoperative cognitive status is critical for diagnosing and anticipating common postoperative complications such as postoperative delirium (POD) or cognitive dysfunction (POCD). Preexisting cognitive impairment predicts POD [25,26]. Postoperative cognitive impairment is associated with longer hospital stay, increased mortality, and functional decline. Explanations may be that patients with impaired cognition are less likely to engage in postoperative aggressive pulmonary hygiene and ambulation, causing a high risk of developing postoperative complications such as pneumonia, deep vein thrombosis, stroke, and cerebrovascular accident with neurologic deficit.

Cardiac evaluation

Diminished cardiac reserve in elderly patients often manifests as exaggerated drops in blood pressure during induction of general anesthesia (GA). Reductions in the responsiveness of beta-receptors caused by a beta-blocked state limits patients’ ability to increase cardiac output and properly respond to blood losses. Baroreceptor dysfunction and reduced responsiveness to angiotensin II further limit responsiveness to hypovolemia. All these factors may be compounded by comorbid myocardial ischemia related to atherosclerosis.

Assessing the metabolic equivalents (METS) of daily activities is a useful way to assess exercise tolerance for patients who may not participate in regular exercise. Geriatric patients should undergo cardiac tests and risk stratification and evidence-based optimization strategies should be applied before surgery [27]. The web-based ACS National Surgical Quality Improvement Program (NSQUIP) Risk Calculator is one of the recommended tools in the 2014 American College of Cardiology/American Heart Association Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery [27]. However, critical knowledge gaps remain for informed decision-making and recommendations targeting older patients. A 2016 study highlighted a critical need for large population-based studies including a broad spectrum of older patients [28]. A 2002 prospective study of 513 patients ≥ 70 years old undergoing non-cardiac surgery showed that abnormalities in preoperative electrocardiogram (ECG) are common but non-specific and thus are of limited value in predicting postoperative cardiac complications compared to the presence and severity of comorbidities [29]. Conversely, echocardiography may help provide insights into ventricular function and valve status; it may be considered in patients with significant cardiac comorbidities such as history of myocardial infarction (MI), congestive heart failure (CHF), or valvular heart disease.

Older patients are more vulnerable to perioperative cardiac ad-
verse events. A 2018 retrospective study of 8,441 adult patients who underwent general and vascular surgeries showed that the underlying predictors of cardiac events after surgery included age > 65 years (OR 4.9, 95% CI 3.4–6.9, P < 0.01) [30]. In addition, a 2017 study showed one-year mortality in elderly patients undergoing hip fracture repair to be significantly higher in patients with postoperative atrial fibrillation, even in patients receiving anti-arhythmic therapy [31]. The anesthesia-related cardiac arrest rate is a quality indicator to improve patient safety in the perioperative period. A 2017 systematic review showed that perioperative and anesthesia-related cardiac arrest rates only decreased with a country’s high Human Development Index (HDI), with perioperative cardiac arrest being 4-fold higher in geriatric patients in low-HDI countries compared to that in high-HDI countries [32]. Another 2014 study showed that a large majority of cardiac arrests in older patients were caused by not anesthesia-related factors. The major predictors of intraoperative cardiac arrests were poorer physical status as based on assessment guidelines from the American Society of Anesthesiologists (ASA) and the need for emergency surgery. All anesthesia-related cardiac arrests were medication-related or airway-related, highlighting the importance of preventive strategies [33].

**Pulmonary evaluation**

Pulmonary function declines with age due to loss of both lung and chest wall compliance and oxygen diffusion capacity, especially in smokers, contributing to decline in oxygen uptake and delivery. Age and functional dependence have been identified as the most reliable risk factors for postoperative pulmonary complications (PPC). A 2006 systematic review showed that patient-related risk factors for PPC included advanced age, ASA class 2 physical status or higher, functional dependence, chronic obstructive pulmonary disease, and CHF. In patients undergoing noncardiac surgery, the rates of PPC are 14% and 15% for ages ≥ 65 years and ≥ 70 years, respectively [34]. A 2017 prospective study for PPC, which included 1,202 patients showed that significant PPC risk factors, such as emergency (OR 4.47, 95% CI 1.59–12.56), surgical site (OR 2.54, 95% CI 1.67–3.89), and age (OR 1.03, 95% CI 1.02–1.05) were nonmodifiable [35]. In addition, a 2003 prospective study of 517 patients ≥ 70 years old and undergoing noncardiac surgery showed that 31.7 percent of patients died from renal complications (HR 6.07, 95% CI 2.23–16.52, P < 0.001), cancer (HR 2.44, 95% CI 1.78–3.38, P < 0.001), and pulmonary complications (HR 2.41, 95% CI 1.30–4.48, P = 0.005). These studies showed that pulmonary complications were an independent predictor of mortality in elderly patients [36].

**Depression**

Senility alone is a high risk factor for depression, and the preoperative psychological burden that patients likely suffer may complicate the situation. ACS-AGS guidelines strongly recommend preoperative depression and substance abuse screening using a simple questionnaire [37]. More than 10% of elderly people have depressive symptoms significant enough to warrant clinical intervention [38]. A 2018 prospective cohort study of 1,035 individuals ≥ 70 years old who underwent transcatheter or surgical aortic valve replacement surgery showed that baseline depression (31.5 percent of patients screened positive) was associated with mortality after 1 month (OR 2.20, 95% CI 1.18–4.10) and 12 months (OR 1.532, 95% CI 1.03–2.24). Persistent depression 6 months after the procedure was associated with a 3-fold increase in mortality at 12 months (OR 2.98, 95% CI 1.08–8.20) [39]. Therefore, active multi-disciplinary management of these patients is needed perioperatively.

**Frailty**

Frailty is a syndrome of decreased physiologic reserve and resistance to stressors. According to the Cardiovascular Health Study, with 5,317 participants ≥ 65 years old, the overall prevalence of frailty in this community was 6.9%, with frailty increasing with age and being greater in women than men [40]. A prospective measure of frailty in 594 patients found that preoperative frailty was associated with an increased risk of postoperative complications (intermediately frail: OR 2.06; 95% CI 1.18–3.60; frail: OR 2.54; 95% CI 1.12–5.77), length of stay (intermediately frail: incidence rate ratio 1.49; 95% CI 1.24–1.80; frail: incidence rate ratio 1.69; 95% CI 1.28–2.23), and discharge to an assisted-living facility after previously living at home (intermediately frail: OR 2.54; 95% CI 1.12–5.77), length of stay (intermediately frail: incidence rate ratio 1.49; 95% CI 1.24–1.80; frail: incidence rate ratio 1.69; 95% CI 1.28–2.23), and discharge to an assisted-living facility after previously living at home (intermediately frail: OR 3.16; 95% CI 1.0–9.99; frail: OR 20.48; 95% CI 5.54–75.68). Frailty independently predicted higher rates of postoperative complications in elderly patients [41]. In addition, a 2019 prospective cohort study of 326 geriatric patients who required emergency general surgery showed that a frail status increased the odds ratio of failure to rescue 3 times when compared with a nonfrail status [42]. A 2014 study including 275 subjects ≥ 65 years old showed that the multidimensional frailty score based on CGA is more useful than conventional methods like the ASA classification (area under the receiver operating characteristic curve, 0.821 vs. 0.647, P = 0.01) for predicting all-cause mortality rates in geriatric patients undergoing surgery [43]. According to a 2017 meta-analysis, sarcopenia and frailty seem to have significant adverse impacts on postoperative outcomes [44]. Another 2018 meta-analysis
identified potentially modifiable prognostic factors (i.e., frailty, depressive symptoms, and smoking) associated with developing postoperative complications that can be targeted preoperatively to optimize care [45]. These results lend support to the view that intensive management of preoperative modifiable factors can prevent postoperative complications.

There is growing evidence that preoperative frailty in elderly patients is associated with increased adverse outcomes after surgery. Although further studies are needed, frailty evaluation will be a useful preoperative risk-stratification tool in perioperative geriatrics [46]. Geriatric specialists will be able not only to make more extensive assessments but also to implement prior rehabilitation measures. Moreover, anesthesiologists should be aware of their role in patient preparation, maintaining or enhancing patient’s functional reserve to facilitate postoperative rehabilitation and discharge back into the society.

**Nutrition**

A 2015 meta-analysis showed that perioperative oral nutritional supplementation had a positive effect on serum total protein and led to fewer complications, such as wound, respiratory, and urinary tract infections, but did not have a positive effect on postoperative mortality [47]. Another clinical trial study showed that perioperative taurine supplementation attenuated postoperative oxidative stress in elderly patients with a hip fracture, but did not improve postoperative morbidity and mortality [48]. However, a 2016 review, which included 41 trials with a total of 3,881 participants, showed that oral multinutrient supplements started before or soon after surgery might prevent complications within the first 12 months after a hip fracture although no clear effects on mortality were seen [49].

Oral nutrition and supplementation counteracted the effects of poor appetite and illness. Prolonged preoperative fasting should be avoided (except in cases with an intraabdominal pathology). Yeniy et al. [50] measured preoperative fasting duration with respect to time of the day and its effect on vital parameters and ECG in elderly patients undergoing surgery under spinal anesthesia (SA). The fasting times were far longer than recommended, with 15-hour fasting being related to a transiently increased cardiac stress and mild hypothermia. Malnutrition is a frequent yet often overlooked problem in the surgical field.

**Polypharmacy**

Geriatric patients usually take various medications, especially cardiovascular and central nervous system acting medications. When compared with younger adults, older people are more likely to have impaired renal function; therefore, it is critical to adjust dosage to prevent adverse effects. The risk of adverse drug reactions increases with the number of drugs taken, leading to more hospital stays [51]. A 2016 analysis of 272 elderly patients with consecutive hip fracture showed that the total number of medications at the time of discharge was predictive of rehospitalization (OR 1.08, 95% CI 1.01–1.17, P = 0.030) but not predictive of mortality [52]. Furthermore, a 2018 meta-analysis showed that comorbidity (Charlson Comorbidity Index ≥ 3) [13], polypharmacy (≥ 5 drugs/day), and ADL dependency were predictive factors for postoperative complications [14]. The ACS/AGS Best Practices Guidelines for the Optimal Preoperative Assessment of the Geriatric Surgical Patients recommended that whenever possible, nonessential medications should be discontinued perioperatively and the addition of new medications should be kept to a minimum [17,53].

For patients at risk of POD, new benzodiazepines [54] and meperidine should be avoided [55,56]. Antihistamine H1 antagonists and strong anticholinergic effective drugs should be cautiously prescribed [54,57]. According to American College of Cardiology/American Heart Association guidelines, beta-blockers are indicated for patients who are already on it or whose known coronary artery disease represents an immediate risk in vascular surgery [58-60]. Beta-blockers should be started days to weeks before elective surgery and titrated to a heart rate of 60 to 80 beats/min in the absence of hypotension. Preoperative statin should be started as soon as possible before surgery for patients who have known vascular disease. For patients undergoing noncardiac surgery and currently taking statins, statins should be continued [60].

Cholinesterase inhibitors (e.g., galantamine, rivastigmine, and donepezil), which are used to slow cognitive decline, was not associated with an increased risk of postoperative respiratory complications among older patients with dementia undergoing hip fracture surgery [61]. Cholinesterase inhibitors may interact with muscle relaxants, thereby prolonging the actions of succinylcholine, reversing the effects of non-depolarizing neuromuscular blocking agents, and leading to larger doses needed to achieve a proper degree of neuromuscular blockade [61,62].

**Anticoagulation therapy**

A 2016 population-based cohort study of 154,047 hip fracture patients showed that 33% of them used one or more antithrombotic on admission, with a higher proportion of men and a higher mean age [63]. In most cases, perioperative bridging anticoagulation is no longer recommended when using novel oral anticoagu-
lants and vitamin-K antagonists [64]. However, this recommendation does not apply to patients at high risk of thromboembolism. Although the use of anticoagulants in the elderly is basically similar with that in younger patients, the reduced renal function frequently seen in elderly patients requires consideration.

Intraoperative Management

Anesthesia in elderly patients

A 2019 meta-analysis showed that postoperative morbidity and mortality increased with age [65]. However, a 2018 meta-analysis showed that laparoscopic hepatectomy is a feasible and safe alternative to open hepatectomy in elderly patients because of the lower rates of morbidity and favorable postoperative recovery and outcomes [66]. Another 2018 meta-analysis showed that the outcomes of laparoscopic gastrectomy for elderly gastric cancer patients were comparable to those in nonelderly patients. A 2017 study showed that laparoscopic liver resection of colorectal liver metastases in subjects ≥ 70 years of age is associated with a significant lower morbidity and a shorter stay [67]. The oncological outcomes were comparable with those in open liver resection even though the benefits of the laparoscopic approach appeared to fade with increasing age. Another recent retrospective study of patients ≥ 80 years old who underwent transabdominal preperitoneal repair of groin hernia showed that the incidence of postoperative complication was influenced by poor performance status, lower hemoglobin level, and lower albumin level rather than old age [68]. Therefore, age alone should not preclude laparoscopic gastrectomy in elderly patients [69].

However, whether old age itself is the only criterion for determining the indication of surgery remains controversial. A 2017 meta-analysis that included 18 studies of pancreaticoduodenectomy in patients ≥ 80 years old showed a higher 30-day postoperative mortality rate (OR 1.51, 95% CI 1.48–3.31, P < 0.001) and length of hospital stay (OR 2.23, 95% CI 1.36–3.10, P < 0.001) in this group of patients compared to that in younger patients. The overall postoperative complication rate was high (OR 1.51, 95% CI 1.25–1.83, P < 0.001) in aged patients [70]. Another recent prospective study including 165 patients who had pancreaticoduodenectomy showed that the 90-day mortality rate (5.9% in those ≥ 80 years old vs. 2% in the younger group, P = 0.333) and the postoperative complication rate (64.7% in the elderly vs. 62.8% in the younger group, P = 0.83) were similar, although the older patients were far more likely to be discharged to a rehabilitation facility than younger patients were (47.1% vs. 12.8%, P < 0.001) [71]. Careful selection of elderly patients and optimal perioperative care, rather than age, should be used to determine whether surgical intervention is indicated. Therefore, the question arises as to whether surgery is associated with a better outcome for the elderly patient when compared with conservative treatment. Ideally, individual parameters should be assessed at an interdisciplinary level, thereby preventing a complication-prone decision-making process based on surgical diagnosis. Once the decision to operate has been made, experienced staffs should be available at all times to anesthetize and operate on the patient as well as to organize appropriate postoperative care.

Mode of anesthesia

To date, there is insufficient evidence to support a single best anesthetic plan for elderly patients. No difference was found in postoperative morbidity, rates of rehospitalization, in-patient mortality, or hospitalization costs in geriatric patients undergoing regional anesthesia (RA) or GA for hip fracture repair [72,73]. GA and RA are both useful for older non-cardiac patients, but for some procedures, e.g., hip fracture surgery, RA seems the technique of choice. The mode of anesthesia may only play a secondary role in mobility, rehabilitation, and discharge delay. There are no specific recommendations regarding the preferred type of anesthesia for elderly non-cardiac patients [74]. Another 2014 population-based retrospective cohort study that included 6,135 age-matched adult pairs with dementia undergoing hip fracture surgery showed that GA and RA are associated with similar rates of most perioperative adverse events (GA, 11.3%; RA, 10.8%, P = 0.44) [75]. The mode of anesthesia also did not have any significant effects on perioperative outcomes (MI, pulmonary complication, stroke, urinary tract infection, and wound infection) after lower extremity amputation in a total of 3,260 geriatric patients [76]. While anesthesia preparation time, start time of surgery, length of surgery, time to sit, and time to walk were shorter in GA, time to fast-track eligibility, phase 1 recovery time, and time to discharge were similar among patients who received SA [77]. Another 2014 retrospective cohort study that included 56,729 patients ≥ 50 years old undergoing hip repair surgery found that RA was not associated with a lower 30-day mortality when compared with GA (RA, 5.4%; GA, 5.8%; instrumental variable estimate of risk difference, -1.1%, 95% CI -2.8 to 0.5, P = 0.20) but was associated with a modestly shorter length of stay. These findings do not support a mortality benefit for RA in this setting [78].

However, a recent retrospective study that included 16,695 geriatric patients and analyzed mortality within 90 days of undergoing hip fracture repair surgery showed that GA and conversion from RA to GA were associated with a higher risk of mortality.
midazolam with propofol sedation in hypoalbuminemia (albumin level below 3 g/dl) geriatric patients under SA found that when compared with midazolam, propofol is associated with greater hemodynamic stability, lesser respiratory depression, and faster recovery [92].

### Anesthetic pharmacology

Standard anesthetic doses can cause more profound clinical effects in the elderly, because of differences in pharmacokinetics and pharmacodynamics with the general population. Lower doses are required for propofol, remifentanil, ropivacaine, and desflurane [93]. Particular care should be taken with hypnotic agents, as the dose required to induce anesthesia is lower but the onset time is prolonged [94]. Depth of anesthesia monitoring is recommended [95,96]. Anesthesiologists should be familiar with potentially inappropriate medications for older patients according to Beers criteria. Thus, for example, elderly people have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents; in general, all benzodiazepines increase the risk for cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in elderly people [53].

**Neuromuscular blocking and reversal agents**

The dose of neuromuscular blocking agents (NMBAs) should hardly be reduced in the elderly for intubation, but their duration of action is often prolonged and difficult to predict along with age-induced changes in pharmacokinetics of long and intermediate-acting NMBAs (especially, aminosteroids including rocuronium and vecuronium), which may cause postoperative residual neuromuscular blockade and associated complications. Therefore, perioperative neuromuscular monitoring including a train-of-four monitoring is strongly recommended [97].

Benzyloquinoliniums including atracurium and cisatracurium have more reliable durations of action because they depend less on renal and hepatic function for their elimination and can thus be favorably considered for use in the elderly [98]. Neostigmine and pyridostigmine are preferable to edrophonium as NMBA reversal agents because their prolonged duration of action can counterbalance that of NMBAs; however, neostigmine reversal may be ineffective or prolonged and standard doses of sugammadex are required in the elderly [93,98].

### Monitoring

The professional association of anesthesiologists recommends...
routinely considering using the following monitoring devices for the elderly, particularly during major or emergency surgery [6].

For intra-arterial blood pressure monitoring, hemoglobin concentration, blood glucose, arterial blood gas testing, and beat-to-beat blood pressure monitoring are recommended. A suitable limit of blood pressure is a fall in systolic blood pressure of more than 20% from pre-anesthesia induction baseline.

For central venous monitoring, catheterization may provide an additional route of venous access after complex surgery when vasoactive drug support is necessary, but its use should be balanced against the possible complication of the procedure. For cardiac output monitoring, there is still limited evidence in the elderly. Because elderly patients have poorly compliant aortas, cardiac output monitoring using Doppler directed at the aorta may provide less accurate information.

For cerebral oxygen saturation, an episode of a decrease in regional cerebral oxygen saturation (rSO₂) of more than 15% of the baseline value is indicative of cerebral ischemia. Ružman et al. [99] evaluated the changes of rSO₂ measured by near-infrared spectroscopy during elective laparoscopic cholecystectomy under TIVA and the association between patient characteristics and critical decline in rSO₂. The rSO₂ was significantly lower in patients older than 65 years, suggesting that monitoring of cerebral oxygenation could be an important part of the perioperative care to prevent cerebral hypoxia in older patients. In addition, early evidence suggests that monitoring of cerebral oxygen desaturation and early intervention may reduce POD or POCD [100].

For depth of anesthesia monitoring, processed electroencephalogram (EEG) neuromonitoring including a bispectral index or entropy monitor is recommended to avoid excessive depth of anesthesia, thereby preventing the development of POD [95,96] or POCD [100] in elderly patients. Lastly, perioperative neuromuscular monitoring is strongly recommended to keep the proper degree of neuromuscular blockade and its safe reversal [97,101].

### Fluid management and blood transfusion

Intraoperative fluid optimization may be associated with benefit in geriatric hip fracture patients. A 2015 systematic review showed that goal-directed fluid therapy during hip fracture repair under SA does not result in a significant reduction in length of stay or postoperative complications [102]. Discharge time was similar in the anesthetist-directed fluid therapy group and the pulse-contour-guided fluid optimization strategy group, as was total length of stay. A nested meta-analysis of 355 patients found non-significant reduction in early mortality (relative risk [RR] 0.66, 95% CI 0.24–1.79) and in-hospital complications (RR 0.80, 95% CI 0.61–1.05) when goal-directed intervention fluid therapy was implemented. However, the study provided preliminary evidence that goal-directed fluid therapy may have a mortality reduction benefit.

A 2014 systematic review including 734 high-risk patients aged 50 years or older found that the use of a cardiac output-guided hemodynamic therapy algorithm did not reduce a composite outcome of complications or 30-day mortality when compared with the usual standard of care [103].

In high-risk surgical patients, several studies have demonstrated that goal-directed hemodynamic therapy (GDHT) significantly reduced postoperative mortality and morbidity [104,105]. However, several studies found that GDHT was not associated with improved cardiac performance and exerted a statistically uncertain risk reduction in postoperative complications in elderly patients [102,106]. Subsequently, a 2016 RCT in patients aged ≥ 70 years old undergoing hip-fracture surgery also indicated that the main GDHT component, the stroke volume maximization by fluid challenges, and traditional pre-anesthesia fluid loading are of questionable value in the elderly [107]. A multicenter RCT involving 807 patients ≥ 75 years old and using a stepped wedge cluster design to assess the effectiveness of an optimization strategy involving GDHT, lung-protective ventilation, and depth of anesthesia monitoring for GA on postoperative morbidity and mortality in high-risk elderly patients undergoing high-risk surgeries (the OPTI-AGED study) identified a considerable gap between clinical practice and the relevant guidelines for anesthetic optimization [108]. Implementation of such multimodal optimization strategies varied independently of factors related to the population or type of surgery, and thus, potential benefit should be further addressed in elderly patients [109].

To date, it is still controversial whether red blood cell (RBC) transfusions might increase the risk of infection after hip fracture surgery in geriatric patients. The Transfusion Requirements In Frail Elderly (TRIFE) randomized study with 284 patients showed that a more liberal RBC transfusion strategy (Hb < 11.3 g/dl; 7 mmol/L) was not associated with higher infection risk in subjects undergoing hip fracture surgery compared to the restrictive RBC strategy group (hemoglobin [Hb] < 9.7 g/dl; 6 mmol/L). The rate of infection was 72% in the restrictive RBC strategy group compared with 66% in the liberal group (RR 1.08, 95% CI 0.93–1.27, P = 0.29) [110]. A 2015 Cochrane review of 2,722 participants between 81 and 87 years old undergoing hip fracture surgery provided preliminary evidence for similar mortality, functional recovery, or postoperative morbidity when using the thresholds for RBC transfusion in the liberal strategy (aiming to maintain a Hb level usually around 10 g/dl) versus the restrictive strategy (based on symptoms of anemia or a lower Hb concentration usually
Lung-protective ventilation

The ACS best practice guidelines for PPC detailed risk factors and strategies to prevent complications. A 2018 expert survey including 362 respondents suggested a care bundle composed of factors before surgery, i.e., supervised exercise programs and inspiratory muscle training; factors during surgery, i.e., low tidal volume ventilation (6–8 ml/kg) with individualized positive end-expiratory pressure (PEEP) of 5–8 cmH₂O and repeated recruitment maneuvers, use of routine monitoring to avoid hypoxia, and efforts to limit neuromuscular blockade; and post-operative factors, i.e., deep breathing exercises and elevation of the head of the bed [115].

Prevention of hypothermia

Elderly patients are vulnerable to perioperative hypothermia, leading to increased morbidity. Especially, during transurethral resection of the prostate (TURP) or bladder tumor (TURB) under SA or GA, or arthroscopic shoulder surgery under GA, it is important to maintain a normal range of body temperature throughout the whole perioperative period. Many studies have therefore been performed to investigate the effects of various active or passive warming devices and methods including a forced-air warming blanket or heated humidifier circuit on perioperative hypothermia or shivering in elderly patients undergoing TURP or TURB under SA or GA and arthroscopic or open urologic surgeries under GA [116-119]. Jo et al. [116] suggested that a brief period of preoperative forced-air warming did not significantly reduce the incidence of intraoperative hypothermia, but it could significantly reduce its severity in elderly male patients undergoing TURP under SA. Moreover, Zhang et al. [120] reported that use of a forced-air warming system combined with an electric blanket was a more effective method for maintaining body temperature compared to individual devices alone in elderly TURP patients.

Hong et al. [117] reported that warming blanket application for 10 min before induction of anesthesia reduced the incidence of hypothermia as measured one hour after induction compared to one-layer cotton blanket. A prospective observational study showed a heated humidifier was more effective in preventing intraoperative hypothermia in elderly patients undergoing open urologic surgeries than a heat moisture exchanger was [118]. A retrospective study performed in arthroscopic shoulder surgery reported that the incidence of postoperative hypothermia was higher and the associated temperature drop was more prominent in geriatric patients compared to young adult patients and suggested that additional warming methods are needed to prevent perioperative hypothermia in geriatric patients [119]. Altogether, these and other studies demonstrated that various warming strategies could be helpful in keeping the body temperature stable in elderly patients undergoing surgery under GA or RA.

Postoperative Management

Postoperative adverse outcomes

Despite the prevalence of preoperative chronic medical conditions, most patients do well postoperatively. Nonetheless, in a prospective cohort study of 544 patients aged 70 and older undergoing non-cardiac surgery, an overall 21 percent of patients developed adverse outcomes and 3.7% died during the in-hospital postoperative period. ASA physical classification, emergency surgery, and intraoperative tachycardia increased the odds of adverse events [121]. Another prospective study of 517 patients ≥ 70 years old and undergoing non-cardiac surgery showed that 31.7 percent of patients were deceased at the time of follow-up and a history of cancer (HR 2.44, 95% CI 1.78–3.38, P < 0.001), ASA physical status > 2 (HR 2.27, 95% CI 1.61–3.21, P < 0.001), neurologic disease (HR 1.59, 95% CI 1.13–2.24, P = 0.008), age (HR 1.42 per decade, 95% CI 1.11–1.81, P = 0.005), postoperative pulmonary complication (HR 2.41, 95% CI 1.30–4.48, P = 0.005), and renal complication (HR 6.07, 95% CI 2.23–16.52, P < 0.001) were all significant independent predictors of decreased long-
term survival [122]. Co-morbid conditions, age, and new hospitalization after discharge were important independent predictors of a long-term decrease in quality of life. To improve postoperative long-term quality of life, geriatric surgical patients should be evaluated for their potential pre- and intra-operative risk factors.

Postoperative transfusion

In a 2016 RCT including 284 frail elderly patients undergoing surgical hip fracture, postoperative transfusion using the liberal hemoglobin target (7 mmol/L, or 11.3 g/dl) improved survival within one year after surgery in the frailest elderly (the nursing home residents) without impairing recovery from physical disabilities and overall quality of life or increasing the risk of infection when compared with the restrictive hemoglobin target (6 mmol/L, or 9.7 g/dl) [123]. According to the Hb thresholds, recovery from physical disabilities in frail elderly hip fracture patients was similar after a restrictive RBC transfusion strategy (Hb < 9.7 g/dl; < 6 mmol/L) and after a liberal strategy (Hb < 11.3 g/dl; < 7 mmol/L). The 90-day mortality rate was higher for the nursing home residents in the restrictive transfusion group (36%) than for those in the liberal group (20%) (HR 2.0, 95% CI 1.1–3.6, P = 0.010). Implementation of a liberal RBC transfusion strategy in nursing home residents has thus the potential to increase survival [124].

Perioperative analgesia

Elderly patients are often undertreated for pain. Acute pain management in the elderly is challenging, with physiological frailty, medical comorbidities, and cognitive impairment commonly compounding pain assessment and treatment. A 2003 retrospective cohort study including 8,855 subjects aged 16 years and older showed that the risk of respiratory depression after short-term opioids use increased with age, substantially after 60 years of age [125]. A 2014 review suggested that multimodal drug therapy and perioperative regional analgesia can be very effective for perioperative pain management in elderly patients [81]. Paracetamol is safe and considered first-line therapy. Nonsteroidal anti-inflammatory drugs should be used with caution because they can cause gastric and renal damage. Although morphine is effective, cautious administration to elderly patients with poor renal or respiratory function and impaired cognition must be taken into consideration.

RA as part of multimodal perioperative treatment can often reduce postoperative neurological, pulmonary, cardiac, and endocrine complications. RA or analgesia has not been proven to improve long-term morbidity but does benefit immediate postoperative pain control. In addition, multimodal drug therapy utilizes a variety of nonopioid analgesic medications in order to minimize dosage and prevent adverse effects from opioids while maximizing analgesic benefit [81]. A 2018 review showed that comprehensive pain protocols for elderly hip fracture patients are required, with fascia iliaca blocks as a local anesthesia method of choice [126]. Ultrasound-guided regional anesthesia/analgesia is an important part of anesthesia practice in the elderly population, the growth of which will continue to outpace that of the younger population due to improvements in lifespan worldwide [127]. In a 2016 RCT comparing ultrasound-guided continuous femoral nerve block versus continuous fascia iliaca compartment block in 60 elderly patients undergoing hip replacement surgery, both ultrasound-guided blocks provided effective anesthesia and postoperative analgesia [128]. Moreover, in a 2014 RCT comparing the hemodynamic effects of combined PCSNB with CSA in elderly high-risk patients undergoing hip replacement surgery, PCSNB produced satisfactory-quality anesthesia in elderly high-risk patients with fewer hemodynamic changes compared with CSA [91].

Another RCT showed that after a major abdominal surgery in the elderly patient, patient-controlled analgesia, regardless of the route (epidural or parenteral), was effective. Furthermore, patient-controlled epidural analgesia using local anesthetics and an opioid provided better pain relief and improved mental status and bowel activity when compared with intravenous patient-controlled analgesia [129].

Postoperative delirium

POD is a common serious postoperative complication, especially in older people, and is associated with increased mortality, morbidity, and health costs. The overall prevalence of delirium in older patients after surgery has been estimated to be 10% [130]. One study in which 144 patients > 50 years were scheduled for an operation requiring a postoperative intensive care unit (ICU) admission showed that 44 percent of patients developed delirium [131]. A recent review of 35 selected articles showed that the incidence of POD was up to 50% [132]. However, a 2015 study including 459 elderly patients found that incident POD was not significantly associated with decreased survival after hip fracture repair and that survival was a function of age at the time of surgery, illness severity based on ASA physical status, and duration of ICU stay after surgery [133].

Among the risk factors for POD, preexisting cognitive impairment and dementia are the strongest predisposing factors [131, 134]. A 2006 study including 333 elderly patients undergoing noncardiac surgery found that 46 percent of patients developed...
POD. By multivariate logistic regression, age (OR 2.5, 95% CI 1.5–4.2) and moderate (OR 2.2, 95% CI 1.2–4.0) or severe (OR 3.7, 95% CI 1.5–9.0) preoperative resting pain were important contributing factors [135]. Therefore, adequate opioid-reduced analgesia is of great importance. A 2019 review suggested that a clinical trial on the usefulness of the STOP-BANG questionnaire on obstructive sleep apnea as a preoperative stratification for POD showed no difference between the low-risk group and the intermediate-to-high risk groups in POD incidence, duration of delirium, and length of ICU. However, a higher preoperative risk for obstructive sleep apnea was associated with a 3-fold higher risk for POD and coma [136]. A retrospective study that included 318 elderly patients undergoing total knee arthroplasty also showed that preoperative dementia is the most important risk factor for POD, suggesting that those patients should be thoroughly evaluated and their dementia should be managed preoperatively. Adequate management of intraoperative hypotension and preoperative hemoglobin might also be helpful in reducing the incidence of POD [137].

A 2018 systematic review, which included 104 studies found no evidence of anesthesia types (GA vs. RA) influencing POD [138]. Another 2018 RCT, which included 256 patients ≥ 75 years old, found that Xenon anesthesia did not reduce the incidence of POD (Xenon; 9.7%, 95% CI 4.5–14.9, sevoflurane; 13.6%, 95% CI 7.8–19.5, P = 0.33) [139]. Meanwhile, a comparison of RA with GA on POD in elderly patients is underway in nine clinical trial centers in China with an expected total enrollment of 1,000 patients [84].

Intraoperative EEG waveform suppression, which often suggests excessive GA, has been associated with POD, prompting research on whether EEG-guided anesthetic administration decreases the incidence of POD. A 2019 systematic review for prevention of POD in elderly patients planned for elective surgery offered preliminary evidence that multicomponent interventions (i.e., comprehensive multidisciplinary care and multimodal interventions), antipsychotics, bispectral index-guidance, and dexmedetomidine treatment can successfully reduce POD incidence in elderly patients undergoing elective non-cardiac surgery [95]. However, recently, a remarkable large-scale RCT of 1,232 adults aged 60 years and older undergoing major surgery showed that EEG-guided anesthetic administration, compared with standard care, did not decrease the incidence of POD. This finding does not support the use of EEG-guided anesthetic administration for decreasing the incidence of POD [140]. Another 2019 RCT with 200 elderly patients undergoing hip fracture repair with SA supplemented with propofol sedation found that heavier intraoperative sedation was not associated with significant differences in mortality or return to pre-fracture ambulation up to one year after surgery [141]. Therefore, further large-scale and well-designed RCTs are needed to clarify the association between EEG-guided anesthetic administration or depth of anesthesia, and POD incidence.

A 2012 clinical trial that included 171 elderly subjects with hip fracture found that delirium episodes and cognitive decline during hospitalization were common, but inpatient geriatric consultation teams intervention reduced the incidence of POD (control group 53.2%; intervention group 37.2%; OR 1.92, 95% CI 1.04–3.54, P = 0.04). However, another study found that geriatric consultation had no effect on the severity or duration of POD episodes [142]. Although the results are not conclusive, a close collaboration with the geriatric team can be useful [143]. A 2017 meta-analysis that included 1,840 elderly patients concluded that comprehensive geriatric care may reduce the incidence of POD (OR 0.71, 95% CI 0.57–0.89, P = 0.003) [144].

Two systematic 2019 meta-analyses of RCTs showed that in elderly patients undergoing noncardiac surgery, perioperative administration of dexmedetomidine, compared with placebo, reduced the incidence of POD [145,146]. In contrast, a 2019 double-blinded, multi-center, randomized study that included 164 elderly patients undergoing cardiac surgery reported that dexmedetomidine-based GA resulted in reduced extubation time and postoperative morphine requirements when compared with propofol-based GA, but no significant difference was observed in POD incidence [147].

If possible, drugs that precipitate POD such as opioids, antihistamines, atropine, sedative hypnotics, and corticosteroids should be avoided in patients at risk, including benzodiazepine [54,148].

**Postoperative cognitive dysfunction**

POCD is another frequent neurologic complication occurring in geriatric patients. The type of anesthesia or analgesia and patient inflammatory response may contribute to POCD. A 2014 clinical trial that included 200 elderly patients with mild cognitive impairment showed that there is no difference in the incidence of POCD at 7 days after radical rectal resection under sevoflurane (33.3%) or propofol-based (29.7%) GA, even though sevoflurane had more severe impact on cognitive function than propofol [149]. However, a 2015 clinical trial that included 90 elderly patients scheduled for resection of an esophageal carcinoma showed the incidence of POCD was higher in sevoflurane than propofol anesthesia using the Mini Mental State Examination (MMSE) and the Montreal cognitive assessment (MoCA) scores. Furthermore, elevated plasma concentrations of TNF-α, interleukin (IL)-6, and S-100β protein were found in patients receiving sevoflurane anesthesia throughout the first postoperative week [150]. However, a
2016 RCT that included 80 elderly patients scheduled for a non-cardiac operation found a negative influence by sevoflurane anesthesia on the early (48 hours postoperatively) and late (9 months postoperatively) state compared to propofol anesthesia and no difference in inflammatory markers (IL6, IL10, TNF-α) between the two anesthesia groups [151]. A 2018 clinical trial that included 120 elderly scheduled for esophageal carcinoma resection showed that POCD incidence was higher in elderly patient receiving sevoflurane anesthesia while dexmedetomidine could alleviate POCD through decreasing TNF-α and IL-6 [152].

A 2018 RCT compared the effect of GA and SA on the occurrence of POCD up to postoperative 30 days in elderly patients undergoing hip fracture surgery and reported that the choice of anesthesia modality did not appear to influence the emergence of POCD in the elderly patients [153]. Meanwhile, a 2019 RCT with 80 elderly patients undergoing orthopedic surgery concluded that compared with GA, SA can effectively reduce eye opening and language presentation times and also has few negative impacts on the short-term cognitive function and mental status of elderly patients, along with lower incidence of POCD [154].

A 2017 RCT was performed to observe whether combined GA and RA affected perioperative cognitive trajectory compared to only GA in elderly patients with arthroplasty [155]. Postoperative MMSE was significantly higher in the combined anesthesia group as well as significantly improved compared with preoperative MMSE score in both groups. Combined GA and RA protected perioperative cognitive trajectory, providing evidence supporting the combined use of RA and GA in elderly orthopedic patients vulnerable to POCD.

A 2016 meta-analysis including 13 RCTs of GA showed that dexmedetomidine significantly reduced the incidence of POCD (RR 0.59, 95% CI 0.45–2.95) and improved the MMSE score (mean difference [MD] 1.74, 95% CI 0.43–3.05) on the first postoperative day and reduced the incidence of POCD thereafter (MD 2.73, 95% CI 1.33–4.12) [156]. Another 2019 meta-analysis including 26 RCTs found that perioperative dexmedetomidine treatment significantly reduced the incidence of POCD (pooled ORs 0.59, 95% CI 0.45–2.95) and improved MMSE score (standardized mean difference [SMD] 1.74, 95% CI 0.43–3.05) on the first postoperative day and decreased IL-6 (SMD: -1.31, 95% CI: -1.87 to -0.75, P < 0.001) and TNF-α (SMD: -1.31, 95% CI: -1.87 to -0.75, P < 0.001) and TNF-α (SMD: -2.14, 95% CI: -3.14 to -1.14, P < 0.001) when compared with saline treatment [157]. A 2016 clinical trial with 134 elderly patients undergoing total knee arthroplasty found that parecoxib sodium decreased POCD incidence and plasma IL-1β, IL-6, and TNF-α levels, suggesting that parecoxib may influence POCD incidence through suppression of inflammation and pain [158]. Another clinical trial in 2017 that included 152 elderly patients scheduled for shoulder arthroscopy showed that parecoxib sodium pretreatment combined with dexmedetomidine could reduce the incidence of early POCD and yielded higher jugular venous oxygen partial pressure and jugular venous oxygen saturation values at postoperative day one when compared with the control group. This effect may be related to the improvement of postoperative analgesia and cerebral oxygen metabolism [159].

In a prospective randomized double-blinded controlled study, the effect of remifentanil and fentanyl on POCD and cytokine levels were investigated in elderly patients undergoing major abdominal surgery. The two opioid groups were comparable in terms of POCD incidence; however, IL-6 levels were lower at the seventh day after surgery in the remifentanil group, suggesting that remifentanil did not reduce POCD compared to fentanyl [160].

Enhanced inflammation response has been increasingly reported in association with POCD [161]. Glucocorticoid receptor (GR) signal plays a key role in suppression of inflammation. In a 2010 prospective cohort that included 126 elderly patients undergoing hip fracture surgery with GA, plasma cortisol levels and the expression levels of GR and FK506 binding protein 51 (FKBP51) in leukocytes were determined from one day before surgery and to up to seven days after surgery. When compared with non-POCD patients, visual analogue scale (VAS) scores at 12 hours after surgery were higher in POCD patients. No significant difference in expression levels of GR was found between POCD and non-POCD patients, but high expression of FKBP51 in leukocytes and glucocorticoid resistance were associated with POCD in aged patients following hip fracture surgery [162].

A 2017 RCT reported that preoperative oral melatonin supplementation might improve early POCD in elderly patients undergoing hip arthroplasty, suggesting that the restoration of normal circadian function with good sleep quality may be a key factor in preventing or treating POCD [163].

To manage POCD, care bundles and protocols for the perioperative period may improve outcomes in the elderly patient. However, to date, there is no clear strategy to improve POD or POCD. Preventive strategies, early recognition, and management of perioperative risk factors seems to be the best modality to treat POCD until further progress is made [164]. Meanwhile, in Germany, a stepped-wedge cluster randomized (PAWEL) trial for the reduction of delirium and POD risks after elective procedures in adults > 70 years old is now planned with an expected 1,500 patients to enroll. Results of the trial should form the basis of future standards for preventing delirium and POCD in surgical wards [165].

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Prevention of postoperative pulmonary complications

Pulmonary complications increase the risk of mortality after surgery and age is a significant risk predictor of pulmonary complications [34,166]. A large retrospective cohort study that included 8,920 elderly patients with hip fracture repair patients found that cardiac and pulmonary complications were most frequent (8% and 4% of patients, respectively) [167].

Well-documented risk factors for pulmonary complications include atelectasis, pneumonia, and pulmonary thromboembolism, advanced age, poor general health status, current infections, pre-existing cardiopulmonary diseases, hypoalbuminemia, and renal dysfunction. Interventions such as lung expansion maneuvers and thromboprophylaxis are effective in reducing the risk of pulmonary complications [168]. According to a 2006 systematic review that included 20 RCTs and 11 meta-analyses not limited to the elderly patient, lung expansion therapy (i.e., incentive spirometry, deep breathing exercises, and continuous positive airway pressure) reduces postoperative pulmonary risk after abdominal surgery. Well-designed trials are needed to clarify the magnitude of benefit and the comparative effectiveness of different modalities [169].

In a 2019 RCT with 76 elderly patients scheduled for hip joint surgery investigating whether pressure-controlled ventilation-volume guaranteed (PCV-VG) may result in better lung ultrasound score (LUS) by reducing atelectasis in the dependent areas of the lung and minimizing respiratory deterioration after surgery in elderly patients compared with volume-controlled ventilation (VCV), PCV-VG showed better LUS results as well as higher dynamic compliance and lower inspiratory peak pressure compared to VCV [170].

Prevention of urinary tract infections

In a 2019 retrospective cohort study in which 221 female patients (age 85.3 ± 7.0 years) with a history of hip surgery, urinary retention occurred in 34 out of the 221 cases (15.4%) and was significantly associated with cognitive impairment (OR 4.11, 95% CI 1.53–11.03, P = 0.005) and ADL (OR 2.61, 95% CI 1.11–6.18, P = 0.029), under adjustment with age and body mass index (BMI). This study demonstrated that cognitive function and ADL were important risk factors for urinary retention, and suggested that the postoperative management of urinary retention is important when considering neurofunctional assistance and nursing care in daily living, especially in elderly female patients undergoing surgery after femoral neck and trochanteric fractures [171]. A 2014 clinical study of risk factors for urinary retention including 72 female elderly patients undergoing hip surgery showed that the early removal of the urethral catheter (per 1-day indwelling period increase, OR 0.33, 95% CI 0.11–0.96, P = 0.04) and preoperative dementia and/or delirium (OR 10.4, 95% CI 1.21–89.2, P = 0.03) had significant correlations with postoperative urinary retention. Femoral neck fractures and the surgical procedure used for the hip surgery did not induce damage to the bladder and nerves involved in voiding function, with the voiding function being recovered in all the patients after short-term intermittent catheterization [172]. Older adults are at particular risk for urinary tract infection, and indwelling urinary catheters should not be used as a substitute for adequate nursing care of incontinent patients.

Conclusion

The main aims of effective perioperative care in elderly patients are to improve the likelihood of them returning to their pre-morbid conditions and maintaining their presence in the community. The perioperative care of elderly patients requires optimization through a multidisciplinary approach that includes risk stratification models. However, the aforementioned approaches are time-consuming and remain a challenge in clinical routine because of limited human resources and lack of funding from healthcare systems. Moreover, the evidence base to inform perioperative care for elderly patients remains poor. More RCTs are needed to clarify the efficacy of GA versus RA for surgery. There are no clear care bundles and protocols, which improve POD or POCD. Preventive strategies and early recognition and management of perioperative risk factors seem to be the best modality until there is further progress in therapeutic interventions. Anesthetic techniques to manage appropriate hemodynamic status during the perioperative period to avoid ischemic complications are required. Anesthesiologists must participate in discussions on the utility of surgery and resuscitation and are strongly encouraged to participate in national surveys and outcomes research. We hope that health care practitioners will use this information to improve their daily practice and that additional research will be undertaken to further improve our future.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Byung-Gun Lim (Conceptualization; Data acquisition and analy-
sis; Investigation; Methodology; Writing—original draft; Writing—review & editing)
Il-Ok Lee (Conceptualization; Data acquisition and analysis; Investigation; Methodology; Supervision; Validation; Writing—original draft; Writing—review & editing)

ORCID
Byung-Gun Lim, https://orcid.org/0000-0002-3302-1831
Il-Ok Lee, https://orcid.org/0000-0001-8062-1496

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anaesthesia in the elderly. Drugs Aging 2016; 33: 765-77.


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Appendix

Appendix 1. Search strategies and items found for each database

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Preoperative risk factors for massive transfusion, prolonged ventilation requirements, and mortality in patients undergoing liver transplantation

Dennis Danforth¹, Rodney A. Gabriel¹², Anthony I. Clark¹, Beverly Newhouse¹, Swapnil Khoche¹, Sanjana Vig¹, Ramon Sanchez¹, Ulrich H. Schmidt¹

Departments of ¹Anesthesiology, ²Biomedical Informatics, University of California San Diego, La Jolla, CA, USA

Background: Despite improvements in techniques and management of liver transplant patients, numerous perioperative complications that contribute to perioperative mortality remain. Models to predict intraoperative massive blood transfusion, prolonged mechanical ventilation, or in-hospital mortality in liver transplant recipients have not been identified. In this study we aim to identify preoperative factors associated with the above mentioned complications.

Methods: A retrospective observational analysis was conducted on data collected from 124 orthotopic liver transplants performed at a single institution between 2014 and 2017. A multivariable logistic regression using backwards elimination was performed for three defined outcomes (massive transfusion ≥ 10 units packed red blood cells (PRBC), prolonged mechanical ventilation > 24 h, and in-hospital mortality) to identify associations with preoperative characteristics.

Results: Statistically significant (P < 0.05) associations with massive transfusion ≥ 10 units PRBC were hepatocellular carcinoma and preoperative transfusion of PRBC. Significant associations with prolonged mechanical ventilation > 24 h were hepatitis C, alcoholic hepatitis, elevated preoperative alanine aminotransferase, and hepatorenal syndrome. Male gender was protective for requiring prolonged mechanical ventilation. End-stage renal disease and hepatitis B were significantly associated with increased in-hospital mortality.

Conclusions: This study identified risk factors associated with common perioperative complications of liver transplantation. These factors may assist practitioners in risk stratification and may form the basis for further investigations of potential interventions to mitigate these risks.

Keywords: Artificial respiration; Blood transfusion; Hepatitis C; Hepatocellular carcinoma; Liver cirrhosis; Liver transplantation.

Introduction

Liver transplantation has become an effective life-saving procedure for patients with acute liver failure, end-stage liver disease, and hepatic malignancy. Despite this, there are many perioperative complications that arise during liver transplantation that contribute to perioperative mortality [1]. The Model for End-Stage Liver Disease (MELD) score has been useful in predicting mortality in patients awaiting liver transplantation [2,3]. However, the MELD score has been shown to have non- or low-predictive value for many complications, including intraoperative massive blood transfusion [4,5] and prolonged mechan-
ical ventilation [6]. Models similar to the MELD score to predict intraoperative massive blood transfusion, prolonged mechanical ventilation, or in-hospital mortality in liver transplant recipients have not been identified [7–10]. We aimed to identify preoperative factors associated with massive transfusion ≥ 10 units packed red blood cells (PRBC), prolonged mechanical ventilation > 24 h, and in-hospital mortality in liver transplant recipients by conducting a retrospective review of comorbidities, preoperative abnormalities, and laboratory values. We hypothesized that specific pre-operative patient characteristics would be associated with the above mentioned complications.

Materials and Methods

Study sample

Data were collected retrospectively from the data warehouse of the University of California, San Diego (UCSD) Healthcare Systems. All data from surgical patients undergoing orthotopic liver transplantation from April 2014 to August 2017 were extracted. The resulting dataset remained de-identified and did not contain sensitive patient-health information as defined by the UCSD Human Research Protections Program, and therefore, was exempt from the informed consent requirement and approved by our Institutional Review Board (IRB), IRB number 171557. During the study period there was no change in surgery or anesthesia leadership of the liver transplant program.

Data and outcomes

The outcomes studied were intraoperative massive transfusion ≥ 10 units PRBC, prolonged mechanical ventilation > 24 h, and in-hospital mortality. Through literature review and expert discussion, we pre-determined factors potentially associated with these outcomes. Characteristics collected for analysis included patient age, sex, body mass index, MELD score, etiology of liver failure (hepatitis C, hepatitis B, alcohol use, hepatocellular carcinoma [HCC], primary biliary cirrhosis, non-alcoholic steatohepatitis [NASH], cryptogenic, and ‘other’), comorbidities (hepatorenal syndrome, hepatopulmonary disease, atrial fibrillation, congestive heart failure, portopulmonary hypertension, coronary artery disease, end-stage renal disease, diabetes mellitus, coagulopathy, cardiac valve abnormality, pulmonary hypertension, and diastolic dysfunction), preoperative laboratory values, and need for preoperative transfusion of PRBC, fresh frozen plasma, cryoprecipitate, and platelets.

Statistical analysis

Statistical analysis was performed using R, a software environment for statistical computing (R Core Team [2013]. R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. Available from http:// www. R-project.org/). A multivariable logistic regression using backwards elimination was performed for each of the three outcomes (transfusion ≥ 10 units PRBC, prolonged mechanical ventilation > 24 h, and in-hospital mortality) to identify associations. All variables were included in the initial model building process of the multivariate analysis. In a step-by-step fashion, we removed one variable at a time from the model that had the highest P value greater than 0.05. This was performed until all variables in the model had P < 0.05 in its association with the outcome. None of the variables that were not statistically significant in its association with the outcome were included in the final model. The odds ratio (OR) and corresponding 95% CI were then reported. Multicollinearity was assessed with variance inflation factor (VIF). We determined that if VIF < 5, correlation between predictor variables were not high. In the multivariable logistic regression analysis, all predictors demonstrated a VIF < 5. When summarizing demographic data, categorical variables were summarized as count and percentages, while continuous variables were reported as mean and standard deviation (SD).

Results

The patient demographics of the 124 patients included in the study are shown in Table 1. The mean age was 55.3 years old (SD 10.7 years). Of the patients, 59.7% were males. Etiologies of liver failure are presented in Tables 1 and 2. Common co-morbidities include diabetes type II, hepatorenal syndrome, congestive heart failure, end-stage renal disease, and coronary artery disease. All liver transplants during the study period were performed by a single primary surgeon. Postoperative outcomes are shown in Table 3: 55.6% of patients required intraoperative massive transfusion ≥ 10 units of PRBC, 53.2% of patients required prolonged ventilation > than 24 h, and 10.5% of patients died during the hospitalization. The mean number of days for postoperative ventilation was 7.8 days (SD 15.5 days). The mean number of days for ICU and hospital length of stay were 8.9 days (SD 13.8 days) and 25.7 days (SD 23.4 days), respectively.

The results of the final multivariable logistic regression model are listed in Table 4 with OR, 95% CI, and P value. Significant risk factors for massive transfusion were HCC and preoperative transfusion of PRBC. Increased preoperative hematocrit, increased pre-
operative fibrinogen, and increased alanine aminotransferase (ALT) were protective for preventing massive postoperative transfusion. Risk factors for postoperative ventilation greater than 24 h included hepatitis C, alcoholic hepatitis, elevated preoperative ALT, and hepatorenal syndrome. Male sex was protective for postoperative ventilation greater than 24 h. Hepatitis B and end-stage renal disease correlated with an increase in in-hospital mortality.

Discussion

Despite orthotopic liver transplantation being the most effective method for survival of liver failure, it carries significant risks of morbidity and mortality. The main findings of our study are: the presence of HCC and preoperative transfusion correlated with intraoperative massive transfusion of ≥10 units of PRBC. Hepatitis C, alcoholic hepatitis, and hepatorenal syndrome correlated with an increased risk of postoperative mechanical ventilation greater than 24 h. Male sex correlated with a reduced risk of prolonged mechanical ventilation greater than 24 h. Hepatitis B and end-stage renal disease correlated with an increase in in-hospital mortality.

Massive transfusion during liver transplantation has been asso-

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### Table 1. Preoperative Characteristics of Cases

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<tr>
<td>Diabetes mellitus</td>
<td>34</td>
<td>27.4</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>4</td>
<td>3.2</td>
</tr>
<tr>
<td>Cardiac valve abnormality</td>
<td>30</td>
<td>24.2</td>
</tr>
<tr>
<td>Pulmonary hypertension (PAP ≥ 25 mmHg)</td>
<td>51</td>
<td>41.1</td>
</tr>
<tr>
<td>Diastolic dysfunction</td>
<td>19</td>
<td>15.3</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Preoperative transfusion</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Packed red blood cells</td>
<td>41</td>
<td>33.1</td>
</tr>
<tr>
<td>Fresh frozen plasma</td>
<td>35</td>
<td>28.2</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>27</td>
<td>21.8</td>
</tr>
<tr>
<td>Platelets</td>
<td>28</td>
<td>22.6</td>
</tr>
</tbody>
</table>

Values are presented as mean (SD) or number of patients (N) and percentage. BMI: body mass index, MELD: model for end-stage liver disease, PAP: pulmonary artery pressure.

### Table 2. Preoperative Laboratory Values

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit (%)</td>
<td>29.4 (7.3)</td>
</tr>
<tr>
<td>Platelets (10⁹/L)</td>
<td>90.0 (99.8)</td>
</tr>
<tr>
<td>INR</td>
<td>2.1 (1.1)</td>
</tr>
<tr>
<td>PTT (s)</td>
<td>45.6 (16.5)</td>
</tr>
<tr>
<td>Fibrinogen (g/L)</td>
<td>1.847 (0.833)</td>
</tr>
<tr>
<td>WBC (10⁹/L)</td>
<td>7.8 (5.5)</td>
</tr>
<tr>
<td>BUN (mmol/L)</td>
<td>8.32 (7.11)</td>
</tr>
<tr>
<td>Creatinine (mmol/L)</td>
<td>0.12 (0.10)</td>
</tr>
<tr>
<td>AST (µkat/L)</td>
<td>2.44 (3.96)</td>
</tr>
<tr>
<td>ALT (µkat/L)</td>
<td>2.29 (7.00)</td>
</tr>
<tr>
<td>Alkaline phosphatase (µkat/L)</td>
<td>2.65 (1.86)</td>
</tr>
<tr>
<td>Albumin (mmol/L)</td>
<td>0.049 (0.09)</td>
</tr>
</tbody>
</table>

Values are presented as mean (SD). INR: international normalized ratio, PTT: partial thromboplastin time, WBC: white blood cells, BUN: blood urea nitrogen, AST: aspartate aminotransferase, ALT: alanine aminotransferase.

### Table 3. Intraoperative and Postoperative Outcomes

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative transfusion requirements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Packed red blood cells (units)</td>
<td>16.3</td>
<td>17.4</td>
</tr>
<tr>
<td>Fresh frozen plasma (units)</td>
<td>12.2</td>
<td>13.1</td>
</tr>
<tr>
<td>Platelets (units)</td>
<td>3.5</td>
<td>3.6</td>
</tr>
<tr>
<td>Cryoprecipitate (units)</td>
<td>5.9</td>
<td>10.8</td>
</tr>
<tr>
<td>Total (units)</td>
<td>37.8</td>
<td>37.9</td>
</tr>
<tr>
<td>Massive transfusion (≥10 units PRBC)</td>
<td>69</td>
<td>55.6</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraoperative</td>
<td>5</td>
<td>4.0</td>
</tr>
<tr>
<td>Postoperative (inpatient)</td>
<td>8</td>
<td>6.5</td>
</tr>
<tr>
<td>Total perioperative mortality</td>
<td>13</td>
<td>10.5</td>
</tr>
<tr>
<td>Postoperative ventilation greater than 24 h</td>
<td>66</td>
<td>53.2</td>
</tr>
<tr>
<td>Intensive care unit length of stay (days)</td>
<td>7.8</td>
<td>15.5</td>
</tr>
<tr>
<td>Hospital length of stay (days)</td>
<td>8.9</td>
<td>13.8</td>
</tr>
</tbody>
</table>

Values are presented as mean (SD) or number of patients (N) and percentage.
ciated with higher mortality, prolonged length of stay, and increased rate of infectious complications [11]. Improvement in intraoperative management has significantly decreased transfusion needs and improved overall mortality and morbidity [12]. Current research has primarily concentrated on intraoperative management. In contrast, we have concentrated on preoperative factors influencing morbidity and mortality of liver transplant recipients. Our statistical analysis demonstrates that patients with HCC and preoperative transfusion have an increased risk for massive transfusion.

The increased risk of bleeding in HCC patients is likely due to the rich blood supply of the tumor. The high pressure of arterial vascularization of the tumor is associated with increased rate of hemorrhage and difficulty obtaining hemostasis [13]. While this is not a modifiable risk factor, the presence of HCC should alert the transplant team for potential higher transfusion needs.

A recent study by Massicotte et al. [14] revealed that preoperative anemia was associated with a higher risk of transfusion during liver transplant and suggests that optimizing hemoglobin before surgery could be potentially valuable. This is consistent with our finding preoperative anemia and preoperative transfusion to be significantly correlated with high transfusion requirement. This could be that transfusion increases central venous pressure, which has been found to be associated with increased bleeding [14].

We report herein that hepatitis, C alcoholic hepatitis, and hepatorenal syndrome are correlated with mechanical ventilation greater than 24 h. Male sex was found to have reduced the risk of mechanical ventilation greater than 24 h. In a previous analysis of a nationwide database prolonged mechanical ventilation has been associated with increased mortality and graft failure [7]. In this study female gender was also associated with increased need for prolonged mechanical ventilation and the authors attributed this to the fact that female liver transplant patients seem to be older, more frail, and potentially have more advanced liver failure [7].

Numerous studies have examined the association of post-transplant mortality with postoperative decline in kidney function [15–17] and preoperative hepatorenal syndrome [18]. However, these studies did not note the association of hepatorenal syndrome and prolonged ventilation, which we found to be statistically significant. The etiology of this association deserves closer investigation, but one hypothesis may be that the relative hypervolemia and increased capillary permeability of patients with hepatorenal syndrome may lead to increased work of breathing and poor gas exchange post-operatively. This may suggest that increased attention to fluid status intraoperatively may be beneficial.

Prior study of the association of hepatitis C and alcoholic cirrhosis with prolonged ventilation was not found in any of the literature reviewed for this study. Despite the unclear etiology of this association, the presence of hepatitis C or alcoholic cirrhosis may assist with risk stratification and patient planning.

Finally, our data analysis found hepatitis B and end-stage renal disease to have significant association with post-transplant in-hospital mortality. Impaired kidney function and post-transplant mortality has been frequently reported, though most studies found a postoperative decline in kidney function to have a higher association with long-term mortality than measurements of pre-

### Table 4. Multivariable Logistic Regression Modeling Various Outcomes

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Massive transfusion ≥ 10 units PRBC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>5.01 (1.20–21.09)</td>
<td>0.032</td>
</tr>
<tr>
<td>Hematocrit (per 1% increase)</td>
<td>0.93 (0.87–0.99)</td>
<td>0.043</td>
</tr>
<tr>
<td>Incremental fibrinogen (per 0.01 g/L increase)</td>
<td>0.99 (0.99–0.99)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Incremental ALT (per 0.017 µkat/L increase)</td>
<td>0.99 (0.99–0.99)</td>
<td>0.013</td>
</tr>
<tr>
<td>Preoperative PRBC transfusion</td>
<td>6.63 (1.82–24.2)</td>
<td>0.004</td>
</tr>
<tr>
<td>Postoperative mechanical ventilation &gt; 24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>0.43 (0.19–0.98)</td>
<td>0.044</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>2.84 (1.16–6.94)</td>
<td>0.027</td>
</tr>
<tr>
<td>Alcoholic hepatitis</td>
<td>3.36 (1.27–8.92)</td>
<td>0.015</td>
</tr>
<tr>
<td>Preoperative ALT</td>
<td>1.004 (1.0003–1.008)</td>
<td>0.031</td>
</tr>
<tr>
<td>Hepatorenal syndrome</td>
<td>2.53 (1.09–5.86)</td>
<td>0.034</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>10.42 (2.16–50.21)</td>
<td>0.003</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>24.24 (2.03–289.73)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Values are presented as odds ratio (95% CI). ALT: alanine aminotransferase, PRBC: packed red blood cells, OR: odds ratio.
operative function [15–18]. Our finding of an association between end-stage renal disease and in-hospital mortality is not unexpected, given the common postoperative complications seen in patients with end-stage renal disease. A large study of dialysis patients undergoing general surgery utilizing the American College of Surgeons NSQIP database found significantly increased rates of death, thromboembolism, stroke, myocardial infarction, pneumonia, and urinary tract infections [19].

Prior studies of liver transplant outcomes have not found increased mortality rates in patients with hepatitis B as compared to hepatitis C, alcoholic cirrhosis, autoimmune hepatitis, and malignancy [20]. The etiology of our finding of significant association between hepatitis B and in-hospital mortality is unclear. One hypothesis may be that fulminant hepatic failure represents an increased proportion of the hepatitis B patients.

Our results have to be seen within the context of its limitations. This is a retrospective single center study. Though all results may not be generalizable, the study period was chosen due to the stable surgical, anesthesia, and medicine transplant teams, which allowed us to focus on the variables in question without having to account for significant differences in patient care. The study population size of 124 is relatively small, which may have left the study underpowered to identify perioperative associations of smaller effect.

In summary we hope that this study prompts further attempts to improve methodologies for predicting perioperative complications in orthotopic liver transplant patients. Though some conclusions were consistent with the known pathophysiology of comorbidities, such as an association between end stage renal disease and in-hospital mortality, other etiologies remain elusive, such as an association between hepatitis C and prolonged mechanical ventilation. These associations prompt many questions deserving of closer investigation. Further investigations should include a more in-depth analysis, including removal of confounding variables, inclusion and exclusion criteria, and further analysis of postoperative events leading to mortality and prolonged mechanical ventilation. Our goal in this and in future studies is to define and refine specific predictive values, allowing practitioners to have a preliminary system of predicting which patients may have an increased risk of massive transfusion, prolonged mechanical ventilation, and in-hospital mortality.

Acknowledgements

UC San Diego Department of Anesthesiology.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Dennis Danforth (Formal analysis; Writing – original draft; Writing – review & editing)
Rodney A. Gabriel (Formal analysis; Investigation; Methodology; Software)
Anthony I. Clark (Data curation; Formal analysis; Investigation; Writing – original draft)
Beverly Newhouse (Data curation; Formal analysis; Investigation)
Swapnil Khoche (Data curation; Formal analysis; Investigation)
Sanjana Vig (Data curation; Formal analysis; Investigation)
Ramon Sanchez (Conceptualization; Data curation; Formal analysis; Investigation; Supervision)
Ulrich H. Schmidt (Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Supervision; Writing – original draft)

ORCID

Dennis Danforth, https://orcid.org/0000-0002-7369-8724
Rodney A. Gabriel, https://orcid.org/0000-0003-4443-0021
Anthony I. Clark, https://orcid.org/0000-0001-9270-2082
Beverly Newhouse, https://orcid.org/0000-0002-2776-7282
Swapnil Khoche, https://orcid.org/0000-0003-3288-4050
Sanjana Vig, https://orcid.org/0000-0002-6777-9018
Ramon Sanchez, https://orcid.org/0000-0002-8963-1137
Ulrich H. Schmidt, https://orcid.org/0000-0002-4733-2243

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5. Feltracco P, Brezzi M, Barbieri S, Galligioni H, Milevoj M, Carol-


Effect of anesthetic method on incidence of delirium after total hip replacement arthroplasty in South Korea: a population-based study using National Health Insurance claims data

Eun-Ji Choi¹, Yoon Ji Choi², Sang Won Lee², Yun-Mi Choi¹, Hyun-Su Ri³, Ju Yeon Park¹, Soon Ji Park¹, Jung-Min Son³, Yoon Sook Lee²

¹Department of Anesthesia and Pain Medicine, Pusan National University Yangsan Hospital, Yangsan, ²Department of Anesthesiology and Pain Medicine, Ansan Hospital, Korea University College of Medicine, Ansan, ³Department of Biostatistics, Clinical Trial Center, Biomedical Research Institute, Pusan National University Hospital, Busan, Korea

Background: There are various reports on the effects of the anesthetic method on neurologic complications. A population-based study was conducted to estimate the effect of anesthetic method on the incidence of postoperative delirium in patients that underwent total hip replacement arthroplasty in South Korea.

Methods: The Korean National Health Insurance claims database was used to retrospectively identify and analyze 24,379 cases of total hip replacement arthroplasty, defined as patients having a claim record with the operation code ‘N0711’, from January 2008 to December 2017. Patients were divided into two groups, a general anesthesia group (n = 9,921) and a regional anesthesia group (n = 14,458). The incidence of delirium was assessed in cases when patients used medications for delirium, such as haloperidol, chlorpromazine, olanzapine, and risperidone.

Results: Of the 9,921 patients receiving general anesthesia and 14,458 receiving regional anesthesia, 142 (1.43%) and 209 (0.86%) experienced postoperative delirium after total hip replacement arthroplasty, respectively. There was no significant difference between the groups (P = 0.92). In logistic regression analysis, sex (P = 0.038) and patients with acquired immune deficiency syndrome (P = 0.008) were predictors of postoperative delirium.

Conclusions: Our results revealed that the anesthetic method was not associated with the incidence of postoperative delirium. In addition, the results suggest that male patients and patients with acquired immune deficiency syndrome undergoing total hip replacement arthroplasty carefully managed for postoperative delirium after surgery.

Keywords: Delirium; General anesthesia; Korean National Health Insurance claims data; Regional anesthesia; Total hip replacement arthroplasty.

Introduction

Delirium is a complex syndrome that affects 7% to 65% of patients after hip-fracture surgery [1–3]. Patients with postoperative delirium have been independently associated with adverse clinical and economic outcomes such as death, decreased functional outcome, and cognitive decline, as well as higher cost of care and longer hospitalization. Therefore, it is important to characterize perioperative risk factors related to the incidence of postoperative delirium and to optimize the quality of care in patients with total...
hip replacement arthroplasty (THRA).

There have been various reports on the perioperative risk factors of postoperative delirium. The pathogenesis of postoperative delirium is unclear and probably multifactorial. Postoperative hypoxemia, postoperative restorations, metabolic and electrolyte anomalies, and sleep disturbances have been thought to be possible causes, as well as the use of certain drugs such as opioids, anesthetics, anticholinergics, benzodiazepine, antiparkinsonian drugs, and tranquilizers. Mental dysfunction on the third postoperative day and mean SpO₂ on the second postoperative night have also been shown to significantly correlate with postoperative delirium [4].

In particular, there is controversy about the effects of general anesthesia (GA) and regional anesthesia (RA) on the incidence of postoperative delirium after THRA. Elderly patients that received general anesthesia displayed more frequent cognitive impairment during the immediate postoperative period compared with those who received regional anesthesia [5]. The mean score of the Mini-Mental State Examination (MMSE) decreased significantly only in patients who received general anesthesia. According to other reports, however, the use of neuraxial anesthesia during surgery did not reduce the incidence of postoperative cognitive dysfunction compared with general anesthesia [6,7]. Even in elderly patients, there was no significant difference in the incidence of cognitive dysfunction three months after the use of either general or regional anesthesia [8].

Therefore, a population-based study was conducted to investigate the effect of anesthetic method on the incidence of postoperative delirium in patients that underwent THRA in South Korea.

Materials and Methods

This study was approved by the Institutional Review Board of our institution (04-2018-015). We retrospectively extracted claim records from The Korean National Health Insurance (NHI) claims database that included the operation code ‘N0711’ and excluded patients who received more than one anesthesia dose (general anesthesia: ‘L1211,’ ‘L1221,’ or regional anesthesia: ‘L1213,’ ‘L1214,’ ‘L1223,’ ‘L1224’), received multiple surgeries with anesthesia, had multiple traumas and fractures (‘S00–S70,’ ‘S73–99,’ ‘T07,’ ‘T14’), or underwent two or more surgeries within the same hospital stay. A total of 24,379 patient cases from January 2008 to December 2017 were extracted.

Baseline characteristics, surgery, disease, and mortality data of the subjects included in the Korean NHI claims database were extracted. Patients were divided into two groups, patients receiving general anesthesia (‘L1211,’ ‘L1221,’ GA group; n = 9,921) and patients receiving regional anesthesia (‘L1213,’ ‘L1214,’ ‘L1223,’ ‘L1224,’ RA group; n = 14,458).

Patients with hypertension were defined by disease code ‘I10–I15’ and patients with diabetes were defined by disease code ‘E10–E14.’ Patients with cardiac disease, including patients with heart failure, were defined by disease code ‘I50,’ patients with cardiovascular disease were defined by specific disease code ‘V192,’ and patients with ischemic heart diseases were defined by disease code ‘I20–I25.’ Patients with respiratory diseases, including patients with chronic pulmonary disease, were defined by disease code ‘J44’ and patients with asthma were defined by disease code ‘J45.’ Patients with Parkinson’s disease were defined by disease code ‘G20–G21’ and patients with mental and behavioral disorder (mood) were defined by disease code ‘F30–34, F38, F39.’ The patient’s disease associated with Charlson comorbidity index was evaluated [9–15].

The diagnosis of patients undergoing THRA was classified into six categories: necrosis with disease code ‘M187,’ unspecified hip arthropathy with disease code ‘M16,’ femur fracture with disease code ‘S72,’ other arthropathy with disease code ‘M19,’ other arthritis with disease code ‘M13,’ and etc.

The incidence of delirium was assessed in cases when diagnosis codes ‘F05.8,’ ‘F05.9,’ ‘F05,’ or ‘F05.0’ were newly added after the operation, or when patients used delirium medications such as haloperidol, chlorpromazine, olanzapine, and risperidone.

Statistical analysis

Data were expressed as mean ± standard deviation, median (25 to 75 percentile), or number of patients (%). The normality test was performed with Shapiro-Wilk W test or Kolmogorov-Smirnov. Baseline and peri-operative characteristics and variables for postoperative outcomes were compared using the independent t-test or the Wilcoxon rank-sum test for continuous variables and the χ² test or Fisher’s exact test for categorical variables. To identify factors significantly predictive of postoperative delirium, univariate and multivariate logistic regression analyses were performed. All statistical analyses were conducted using SAS® ver. 9.4 (SAS Institute, USA). A P value < 0.05 was considered statistically significant.

Results

A total of 24,379 cases of patients undergoing THRA were extracted from the NHI claims database, as shown in Fig. 1. The total number of patients undergoing THRA increased annually, and since 2011, patients were approximately 1.5 times more likely to
undergo THRA under regional anesthesia than general anesthesia (Fig. 2, P < 0.05). Among the patients undergoing THRA, 1,521 (15.33%) of the patients who received general anesthesia and 2,548 (17.61%) of the patients who received regional anesthesia were aged 65 years and older (Fig. 3).

Demographic data are shown in Table 1. In patients undergoing THRA, males (P = 0.003) and elderly patients (P < 0.001) were more likely to undergo regional anesthesia. Patients with cardiac disease were more likely to undergo general anesthesia (P = 0.004), and no difference in the anesthetic method was observed in patients with respiratory (P = 0.975) or cerebrovascular disease (P = 0.121). GA group were found to have a higher score of Charlson comorbidity index than RA group (P < 0.001).

The most common diagnosis was necrosis in patients undergoing THRA (Table 2, P < 0.001). The duration of hospital stay was longer in the RA group than in the GA group (P < 0.001), and the cost of treatment was higher in the GA group than in the RA group (P < 0.001). The mortality rate during hospitalization did not differ according to the anesthetic method (P = 0.448). Of the 9,921 GA group and 14,458 RA group, 142 (1.43%) and 209 (0.86%) experienced postoperative delirium after THRA, respectively. There was no significant difference in the incidence of postoperative delirium between the groups (P = 0.92).

In Table 3, sex, myocardiac infarction, chronic pulmonary disease, peripheral vascular disease, mild liver disease, acquired immune deficiency syndrome (AIDS) were related with postoperative

Fig. 1. CONSORT flow diagram of this study.

Fig. 2. Patients that underwent total hip replacement arthroplasty according to year.

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delirium (P < 0.2). Even in multivariate analysis, sex (P = 0.038) and AIDS (P = 0.008) were related with postoperative delirium. Of the patients with delirium, delirium occurred 1.97 times more frequently in men (233 [66.38%]) than in women (118 [33.62%]).

**Discussion**

Our results revealed that the anesthetic method is not associated with the incidence of postoperative delirium. In addition, our re-
Results showed that patients who experienced postoperative delirium after THRA were more likely to be male and patients with AIDS. The contribution of general anesthesia as an independent risk factor for the development of postoperative delirium remains unclear. In the case of THRA, the choice of anesthesia, general or neuraxial, is decided by the anesthesiologist and is based on the patient’s preference, the clinical experience of the anesthesiologist, comorbidities, and potential postoperative complications.

A previous study [16] showed that general anesthesia with isoflurane and nitrous oxide affects postoperative spatial memory for at least three weeks in aged rats and may adversely influence memory processes in the elderly. It has been suggested that general anesthesia alters brain function, resulting in delirium [16,17]. In fact, during the first three days after surgery, the mean MMSE score was significantly decreased in patients who underwent general anesthesia [5]. Previous studies [18,19] suggest that neuraxial

Table 2. Perioperative Data from Patients That Underwent Total Hip Replacement Arthroplasty

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Group GA (n = 9,921)</th>
<th>Group RA (n = 14,458)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Necrosis (M87)</td>
<td>4,634 (46.71)</td>
<td>7,787 (53.86)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Unspecified hip arthropathy (M16)</td>
<td>1,741 (17.55)</td>
<td>2,618 (18.11)</td>
<td></td>
</tr>
<tr>
<td>Femur fracture (S72)</td>
<td>900 (9.07)</td>
<td>1,439 (9.95)</td>
<td></td>
</tr>
<tr>
<td>Other arthropathy (M19)</td>
<td>274 (2.76)</td>
<td>303 (2.10)</td>
<td></td>
</tr>
<tr>
<td>Other arthritis (M13)</td>
<td>219 (2.21)</td>
<td>418 (2.89)</td>
<td></td>
</tr>
<tr>
<td>etc.</td>
<td>2,153 (21.70)</td>
<td>1,893 (13.09)</td>
<td></td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>17.88 ± 11.96</td>
<td>18.10 ± 11.10</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cost (won)</td>
<td>651.93 (564.35–730.34)</td>
<td>617.25 (545.26–709.31)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Patient charges (won)</td>
<td>128.65 (68.40–149.86)</td>
<td>123.61 (75.71–144.95)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Insurance (won)</td>
<td>526.87 (452.42–600.83)</td>
<td>494.69 (436.03–580.40)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Delirium</td>
<td>142 (1.43)</td>
<td>209 (0.86)</td>
<td>0.927</td>
</tr>
<tr>
<td>Mortality rate during hospitalization</td>
<td>20 (0.20)</td>
<td>36 (0.25)</td>
<td>0.448</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD or number (%). GA: general anesthesia, RA: regional anesthesia, DM: diabetes mellitus.

Table 3. Logistic Regression Analysis of Patients That Underwent Total Hip Replacement Arthroplasty

<table>
<thead>
<tr>
<th></th>
<th>Univariate Odds ratio (95% CI)</th>
<th>P value</th>
<th>Multivariate Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>0.788 (0.631–0.985)</td>
<td>0.037*</td>
<td>0.779 (0.622–0.975)</td>
<td>0.029†</td>
</tr>
<tr>
<td>Anesthetic method</td>
<td>0.990 (0.799–1.227)</td>
<td>0.927</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.000 (0.991–1.009)</td>
<td>0.989</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.935 (0.704–1.242)</td>
<td>0.642</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>0.969 (0.690–1.360)</td>
<td>0.856</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>0.881 (0.523–1.484)</td>
<td>0.633</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.955 (0.862–4.430)</td>
<td>0.108*</td>
<td>1.955 (0.862–4.434)</td>
<td>0.109</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>0.392 (0.122–1.193)</td>
<td>0.097*</td>
<td>0.381 (0.122–1.193)</td>
<td>0.097</td>
</tr>
<tr>
<td>Diagnosis for surgery</td>
<td>0.996 (0.906–1.096)</td>
<td>0.940</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td>&lt; 0.001 (0.011–1.000)</td>
<td>0.968</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>&lt; 0.001 (0.011–1.000)</td>
<td>0.976</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental and behavioral disorder (mood)</td>
<td>1.180 (0.523–2.663)</td>
<td>0.691</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>0.734 (0.181–1.932)</td>
<td>0.596</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>0.481 (0.179–1.292)</td>
<td>0.146*</td>
<td>0.478 (0.178–1.285)</td>
<td>0.144</td>
</tr>
<tr>
<td>Mild liver disease</td>
<td>0.771 (0.557–1.066)</td>
<td>0.115*</td>
<td>0.739 (0.533–1.024)</td>
<td>0.069</td>
</tr>
<tr>
<td>Acquired immune deficiency syndrome</td>
<td>5.590 (1.718–18.220)</td>
<td>0.004*</td>
<td>5.001 (1.532–16.318)</td>
<td>0.008†</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>1.013 (0.887–1.158)</td>
<td>0.845</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD or number (%). DM: diabetes mellitus. *P < 0.15 for univariate-crude data, †P < 0.05 for multivariate-crude data.
anesthesia reduces cortisol hypersecretion and the intensity of postoperative inflammatory response more effectively than general anesthesia, and that epidural analgesia provides better postoperative pain relief than intravenous analgesia. Neuraxial anesthesia and analgesia reduced the occurrence of postoperative complications and mortality, compared to general anesthesia and intravenous analgesia in high risk patients. Furthermore, patients who underwent general anesthesia during THRA showed significant cognitive decline for several months after surgery [20].

Weinstein and colleagues showed that patients who received neuraxial anesthesia were at a lower risk of postoperative delirium, compared with those receiving general anesthesia [21]. As regional anesthesia uses neuraxial blocks, the use of general anesthetic drugs and opiates that can cause delirium after surgery can be avoided [22]. Neuman et al. [23] reported that general anesthesia can sometimes result in severe anesthetic depth and perioperative hypotension, which increases the risk of death. However, regional anesthesia does not completely eliminate the risk of hypotension and sedation before and after surgery [24,25]. Some studies [23,25] suggest that regional anesthesia may reduce the length of hospital stay slightly. Our study also showed that the duration of hospital stay was longer in the RA group than in the GA group. There is also evidence that respiratory complications and intraoperative hypotension are more common in patients receiving general anesthesia.

However, other studies have shown different results. In one study, the perioperative use of benzodiazepines, narcotics, and anticholinergic agents was not associated with postoperative delirium in an elderly cohort of patients undergoing hip surgery [26]. Patel et al. [27] conducted a systematic review of 104 studies, concluding that anesthesia type had no effect on the development of postoperative delirium. Other studies have found no differences in postoperative morbidity, re-hospitalization rates, in-patient hospitalization costs, and mortality for elderly patients receiving regional or general anesthesia for THRA [24,28]. However, these results are lacking an extensive evidence base. Therefore, rigorous studies with appropriate methodology are required to determine the impact of anesthetic method on patient outcome.

Our study is an analysis of data related to postoperative delirium after THRA in a Korean population. The Korean NHI claims database has the great advantage of being the largest available management database that includes all payers. Moreover, all the people in Korea are covered by medical insurance. Therefore, in cases of illnesses, such as delirium, the Korean NHI claims database can be used to conduct research using a large sample size. In our study, it is likely that postoperative delirium after THRA was underdiagnosed because an incidence of 1.43% and 0.86% in the GA and RA group, respectively, is substantially lower than that reported in other studies [1,2]. This may be a result of differences in the methods of diagnosing delirium. We defined delirium as the use of medication for delirium after surgery as it was not possible to diagnose delirium using MMSE or Confusion Assessment Method. Therefore, in our study, the incidence of mild delirium might have been overlooked and, consequently, the incidence of postoperative delirium underestimated.

In addition, the NHI claims database has 97% of the national medical information of the population in Korea, but there are some limitations for clinical research. Because it is not a clinical data, it lacks detailed information about the patient and may be inaccurate because patient information was only collected using the disease code or operation code. In particular, in the case of delirium, factors such as blood pressure during operation, hypoxemia, underlying condition, American Society of Anesthesiologists physical status classification, etc. may be influenced multifactorially. However, the NHI claims database cannot confirm such data. And, data on drug management is in-hospital information, making it difficult to know exactly when to administer the drug.

In conclusion, our results suggest that anesthesia method is not associated with the incidence of postoperative delirium. Therefore, depending on the patient’s condition and the experience of the anesthesiologist, both anesthetic methods should be considered in THRA.

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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Eun-Ji Choi (Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Resources; Software; Supervision; Visualization; Writing – original draft)
Yoon Ji Choi (Conceptualization; Data curation; Funding acquisition; Investigation; Methodology; Project administration; Software; Supervision; Validation; Visualization; Writing – original draft)
Sang Won Lee (Formal analysis; Resources; Writing – review & editing)
Yun-Mi Choi (Investigation; Project administration; Validation)
Hyun-Su Ri (Funding acquisition; Software)
Ju Yeon Park (Data curation; Writing – review & editing)
Soon Ji Park (Formal analysis; Software)
Jung-Min Son (Data curation; Resources)
Yoon Sook Lee (Supervision; Writing – review & editing)

ORCID
Yoon Sook Lee, https://orcid.org/0000-0002-6455-0680
Jung-Min Son, https://orcid.org/0000-0002-6573-7578
Soon Ji Park, https://orcid.org/0000-0002-3417-9972
Ju Yeon Park, https://orcid.org/0000-0002-4642-3717
Hyun-Su Ri, https://orcid.org/0000-0002-7305-4144
Yun-Mi Choi, https://orcid.org/0000-0002-8386-1265
Sang Won Lee, https://orcid.org/0000-0001-9359-2639
Yoon Ji Choi, https://orcid.org/0000-0003-3031-357X
Eun-Ji Choi, https://orcid.org/0000-0003-3731-0785

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Background: The quadratus lumborum block (QLB), which is reported to provide analgesia to the abdominal region, is a newly defined fascial plane block method. The present study aimed to investigate the effect of ultrasound guided anterior QLB on the postoperative pain scores after percutaneous nephrolithotomy (PNL).

Methods: In this prospective, randomized, controlled single-blind study, 60 patients with PNL operations were randomized into 2 groups. In Group B (n = 30): anterior QLB+ intravenous patient-controlled analgesia (PCA) morphine and in Group C (n = 30): intravenous PCA morphine. Outcome measures were included for visual analog scale (VAS) scores and cumulated consumption for 24 hours postoperatively. Adverse effects, additional analgesic requirement, and intraoperative opioid requirement were recorded.

Results: The mean values of the quantity of cumulated morphine used at the 6th, 12th, and 24th hours were found to be statistically significantly lower in Group B (P < 0.05). The VAS scores were found to be statistically significantly lower in Group B (P < 0.05). There were no statistically significant differences in the rate of adverse effects, additional analgesic requirement, and intraoperative opioid requirement between the groups.

Conclusions: The study results suggest that anterior QLB is an effective treatment option for postoperative analgesia of PNL.

Keywords: Fascia; Local anesthetic; Pain; Percutaneous nephrolithotomy; Quadratus lumborum block; Ultrasonography.

Introduction

Recently, the percutaneous nephrolithotomy (PNL) method, which is often described as a minimally invasive procedure, is frequently used in the treatment of kidney stones. In the updated European Association of Urology stone disease guidelines, PNL is recommended as the first choice in kidney stones above 2 cm [1]. Although PNL is applied as a minimally invasive procedure, dilatation of the renal capsule and parenchymal duct, and peritubular distension of the nephrostomy tube were identified as the cause of postoperative pain [2,3].

For postoperative pain, regional anesthesia methods are frequently used as well as intravenous drugs, which are essential because they reduce postoperative complications and hospitalization periods [2–4]. Intercostal block, paravertebral block, and peritubular infiltration are frequently used as regional anesthesia methods. For all 3 methods, lower pain scores or less opioid use was found in the literature compared to intravenous analge-
months. Drug applications [5–7].

Recently, truncal blocks, which can be described as less risky than central blocks, are used for many surgical procedures with ultrasound guidance [8]. The quadratus lumborum block (QLB), which is reported to provide analgesia to the abdominal region, is a newly defined fascial plane block method. Though the application method seemed similar to posterior transversus abdominis plane (TAP) block when it was first defined, the injection site is deeper and more dorsal to transverse abdominis aponeurosis [9,10]. It has been reported that local anesthesia applied between the quadratus lumborum (QL) and thoracolumbar fascia can spread to the paravertebral area due to the anatomical structure of the fascia; and is effective on somatic and visceral pain at the level of thoracic 5 (T5)-lumbar 1 (L1) after the block [8–10]. QLB can be applied as 4 different types called lateral (QLBI), posterior (QLBII), anterior (transmuscular QLB, QLB III), and intramuscular methods [11–14].

In this study, we aimed to investigate the effect of ultrasound-guided anterior QLB applied to the QL muscle on the pain scores and morphine consumption after PNL. We hypothesized that the patients who applied QLB would have lower visual analog scale (VAS) values and lower morphine consumption than the group for which QLB was not applied.

Materials and Methods

A prospective, randomized, controlled, single-blind study was conducted per the Declaration of Helsinki. The approval of the local ethics committee was received, and 70 patients scheduled for a PNL operation were evaluated in terms of the suitability to the study (Local Ethics Committee Ethical number: 2018-1/32, Clinical Trials.gov identifier: NCT03425162).

Patients aged 20–60 years, American Society of Anesthesiologists physical status I–II risk class and undergoing PNL operations were included in the study. Exclusion criteria were the presence of allergies to medications used, not giving consent to participate in the study, the presence of infection at the site of the blockage, and a body mass index (BMI) above 35 kg/m². Sixty patients agreed to participate in the study and received written informed consent. These patients were randomized with a spontaneous numbers table into 2 groups labeled Group B (n = 30): anterior QLB with bupivacaine (20 ml, 0.25%) + intravenous patient-controlled analgesia (PCA) morphine, and Group C (n = 30): intravenous PCA morphine (Fig. 1).

General anesthesia was administered initially intravenously with propofol and rocuronium, and then by inhalation anesthesia with sevoflurane, air, and O₂ mixture, 2.5–3 L/min flow. Analgesia was given as 1 μg/kg fentanyl if needed. The surgical procedure was performed in the prone position.

**Surgical procedure**

Patients were placed prone, and percutaneous access was achieved under fluoroscopy using an 18 gauge (G) needle and

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**Fig. 1.** CONSORT diagram. aQLB: anterior quadratus lumborum block, PCA: patient controlled analgesia.
guidewire. Channel dilatation was performed using Amplatz dilators, and the Amplatz renal sheath was placed in either 30 F or 32 F. We used a nephroscope and a ureteroscope to work with the collection system. Ultrasonic or laser lithotripsy was performed to break up the kidney stones. After collection of all fragments, a 14 F or 16 F reentry nephrostomy tube was placed, and then the procedure was terminated.

Unilateral QLB

Block applications were performed after the operation was completed, while the patient was still under general anesthesia. The patient was placed in a lateral decubitus position such that the side for the operation was on top. A convex ultrasound probe (2-6 MHz MyLab30; Esaote, Italy) was placed on the iliac crest and in the transverse position to the posterior axillary line. Subsequently, the L4 vertebral body at the L4 vertebra level, along with the L4 transverse process, the QL, the erector spinae, and the psoas muscle, were identified as the Shamrock sign (Fig. 2). A 21 G (100 mm) peripheral nerve block needle (Quincke SonoPlex Pajunk, Germany) was directed towards the TLF from the posterior aspect of the transducer to the posteromedial anterolateral direction between the psoas muscle and the QL muscle, anterior to the QL muscle [14,15]. After confirming the site by hydrodissection, bupivacaine was injected with a concentration of 20 ml of 0.25% [14,15] (Fig. 2). Twenty minutes after the operation, 8 mg intravenous tenoxicam was administered for postoperative analgesia, and PCA infusion started. Intravenous morphine infusion was administered as a 0.5 mg bolus and 1 mg loading from the solution prepared with PCA (CADD-Legacy<sup>®</sup> PCA, Smiths Medical, St Paul, USA) at a concentration of 0.4 mg/ml, with a lock time of 20 minutes. Using a cold test, at least 4 dermatomal levels were evaluated for decreased sensory loss compared to a successful contralateral side block at the 30th postoperative minute. If VAS was greater than 4, then 1 g paracetamol (intravenous) was ordered for additional analgesia.

Outcome measures

Primary measures

Primary measurements recorded were the VAS scores (30th min, 2nd, 6th, 12th, and 24th hours post-operation). The patients were informed of the VAS score questionnaire before the operation, and the VAS was explained. The patients marked the level of pain that they felt, using their own hands, on the 10 cm line.

Secondary measures

Secondary measurements recorded were the quantity of cumulated morphine used (at the 2nd, 6th, 12th and 24th hours post-operation), any additional analgesic requirement, side effects such as nausea and vomiting, pruritus, respiratory depression, bradycardia, hypotension, and intraoperative opioid requirement. Further, an investigator, blinded to the patients’ group assignments, evaluated the patients.

Statistical analysis

In addition to the descriptive statistical techniques (frequency,
percentage, mean, standard deviation, median, min-max), a chi-square test was used to compare qualitative data in the evaluation of the study data. A Kolmogorov-Smirnov test was used to test the data for normality; and when normal distribution was detected, the Student's t-test test was used for the inter-group comparisons in this study. Probability (p) values less than α = 0.05 were considered significant and indicative of a difference between the groups. The analysis of the data was performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., USA. Released 2013). The primary outcome measure of this study was a 15% reduction in the control group's VAS scores (7.6 ± 1.26) at 6 hours post-operation [7]. For a study power of 90% (α = 0.05), the calculated required sample size per group was 27, for a total of 54 patients. In order to increase the power of the study and assuming a 10% participant attrition, 30 patients were planned for each group.

**Results**

The study was completed with a total of 60 patients. The demographic characteristics of the patients are shown in Table 1. There was no statistically significant difference between the 2 groups for age, BMI, gender, and the amount of opioid given during the operation (Table 1). There was no statistically significant difference in the cumulative morphine usage between the two groups at the 2nd hour (P = 0.09), but statistically significant differences were found between the 2 groups, which was lower in Group B at other measurement times (Table 2). When VAS scores were examined, there were statistically significant differences at all measurement times (P < 0.001) except 30 minutes (P = 0.109) (Table 3). There was no statistically significant difference in the frequency of side effects, consumption of paracetamol as rescue analgesia, and the duration of the operation between the 2 groups (P > 0.05). No complications were found in any of the patients who underwent block (Table 4).

**Discussion**

After a PNL operation was performed under general anesthesia, we evaluated the efficacy of the anterior QLB group compared with the control group.
to the placebo group. In the QLB group, VAS scores except for the 30th minute postoperative time and morphine consumption except for the 2nd postoperative hour were found to be lower in the other measurement times.

After a PNL operation, postoperative pain, mucosal injury, and inflammation in the renal capsule and collecting system are conducted through sympathetic fibers from the T8–L12 spinal segments, while the sensations of muscle and skin pain are conducted through the intercostal nerves at the T6–T10 level [16]. In the literature, different types of analgesic techniques have been used for PNL operations. Although the intravenous analgesia is the standard technique, regional anesthesia such as a paravertebral block, intercostal block, and nephrostomy tube cannula infiltration have all been used as alternate postoperative analgesia for PNL [2,5,7,17,18].

In the literature, there are studies which successfully used paravertebral block administration for pain palliation. Ak et al. [19], while evaluating postoperative morphine consumption values and VAS scores after the block, found lower opioid use-values. At the time of this study, many other studies have focused on fascial plane blocks that may be an alternative to neuraxial blocks [8–12]. QLB is also a recently used fascial plane block in several types of surgical procedures and for which proper indications must be determined. This block, which initially was used for postoperative pain control after abdominal surgery, has now been used in various operations such as distal lower extremity surgery and nephrectomy pain.

It was reported that QLB block provides analgesia on the lateral and anterior abdominal wall after two different versions of the block were described by Blanco and McDonnell with injection types administered to the QLBI and QLBII of the QL muscle. Afterward, QLBIII was described as an alternative route using a local anesthetic injection administered between the QL and the psoas muscle [14]. The literature information includes clinical studies, cadaver studies, and case reports for different types of QLB block administration [14,20–22].

In studies designed as RCT, Blanco et al. [10,11] used QLB for pain control after cesarean operations in two different studies. In their study with the placebo group, they found less morphine consumption in the QLBI (type 1) group, while in their other study, they compared the results of patients who received QLBII (type II) with those who received a TAP block. In the results of this study, they reported that they provided less morphine consumption and more prolonged analgesia in patients receiving QLB. In another study of a pediatric patient group, Öksüz et al. found a decrease in the requirement for rescue analgesia after a posterior QLB block [23].

In a series of 22 patients who received a substernal anterior QLB block after upper urinary system operations, dermatomal spread and VAS scores were reported. The mean VAS scores of the patients who had a follow-up for 3 days were 3.7 on the 1st day (Range 4 to 5, on a 1–10 scale). The authors of that report opined that these values might be due to previous chronic pain in 3 patients [24]. In our study results, it is remarkable that the mean VAS scores of the group treated with a block were lower than in that earlier study. However, a different type of surgery and relatively less invasive PNL procedures may change the results. The reported results of 1 pediatric and 3 adult patients who received the block for analgesia after open kidney surgery suggest that an anterior QLB block provides successful analgesia [25–27].

Although the studies suggest that QLB provides successful analgesia, there are still unclear issues regarding the block. The first one seems to be the amount of local anesthetic administered. Some studies achieved successful block results after the administration of local anesthetics at doses of 20–30 ml [10,11,24–27]. The amount of local anesthetic that we used (20 ml) achieved a lower VAS score in postoperative pain and lowered morphine consumption values compared to the control group. The other two important points are sensory block level and the mechanism by which the local anesthetic drugs act. The mechanism of action has been focused on for ganglion blockade, sympathetic block, and paravertebral spread [28,29]. In the literature, there are many predictions that drugs administered to the fascial plane may lead to variations in the spread due to biomechanical effects. However, it is also emphasized that there are unresolved indications that use of anesthetized, administration of muscle relaxant, and block administration position may affect the spread.

Further, the data obtained in our study results were not sufficient to discuss the sensory block and mechanism of action. Complications that may arise because of an anterior QLB block depend on the technique and the amount of local anesthetic administered.
Technically, full visualization of the needle tip during the injection is essential due to the closeness of the administration site to the abdominal structures. Since the frequency of using local anesthesia is higher than peripheral nerve block administration, it has been reported that this may cause potential local anesthetic systemic toxicity (LAST) related complications due to systemic absorption [30]. Although it was found that local anesthetic levels after QLB did not reach a toxic dose, we think that further studies are needed to quantify the potential risk [21]. In this study, we administered 20 ml local anesthetics and unilateral block resulting in no clinical occurrences of LAST.

A case report and a study presented in the literature, reported weakness in the lower extremity on the block administration side [22,31]. In the study by Okmen et al. [22], it was found that pneu-moperitoneum established during laparoscopic cholecystectomy might cause this weakness by increasing the drug spread. We found no weakness in the lower extremities and no other complications in patients included in this study who received a block. Lower local anesthetic dose compared to other studies might be a factor.

Limitations of this study are that sensory block level ranges and the block time could not be monitored after block administration, the patients’ follow-up was limited to 24 hours, and the amount of opioid use during the operation varied depending on the patients’ weights (despite attempting to standardize).

The results of this study demonstrate that anterior QLB administered for pain after PNL may be an effective analgesia technique. Determining the analgesic level and duration of action of the block are important opportunities for future research.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Korgün Ökmen (Investigation; Conceptualization; Supervision; Data curation; Writing—original draft; Methodology)
Burcu Metin Ökmen (Formal analysis; Supervision; Writing—review & editing)

ORCID

Korgün Ökmen, https://orcid.org/0000-0001-8546-4661
Burcu Metin Ökmen, https://orcid.org/0000-0002-6242-7048

References


Effect of transportation method on preoperative anxiety in children: a randomized controlled trial

Sun-Hong Park, Sanghee Park, Seongheon Lee, Jeong Il Choi, Hong-Beom Bae, Youngwook You, Seongtae Jeong

Department of Anesthesiology and Pain Medicine, Chonnam National University Medical School and Hospital, Gwangju, Korea

Background: This study was performed to evaluate the effect of a wagon as a transport vehicle instead of the standard stretcher car to reduce children’s anxiety of separation from parents. The secondary goal was to evaluate whether this anxiolytic effect was related to age.

Methods: We divided 80 children (age 2–7 years) into two groups. The stretcher group was transferred to the operating room on a conventional stretcher car, whereas the wagon group was transferred using a wagon. The level of anxiety was evaluated three times using the Modified Yale Preoperative Anxiety Scale (mYPAS): in the waiting area (T0), in the hallway to the operating room (T1), and before induction of anesthesia (T2).

Results: The mYPAS score was significantly lower in the wagon group (36.7 [31.7, 51.7]) than in the stretcher group (51.7 [36.7, 83.3]) at T1 (P = 0.007). However, there was no difference in the mYPAS score between the two groups at T2 (46.7 [32.5, 54.2] vs. 51.7 [36.7, 75.0], respectively, P = 0.057). The baseline anxiety tended to be lower with increasing age (r = −0.248, P = 0.031). During transportation to the operating room, the increase in the mYPAS score (T1-T0) was greater as the age of children decreased in the stretcher group (r = −0.340, P = 0.034). However, no correlation was observed in the wagon group (r = −0.053, P = 0.756).

Conclusions: The wagon method decreased preoperative anxiety, suggesting that it may be a good alternative for reducing preoperative anxiety in children.

Keywords: Anxiety; Child; Operating rooms; Separation; Stretchers; Transportation of patients.

Introduction

In general, children show more severe preoperative anxiety than adults. In addition, children under the age of eight years often show more preoperative anxiety during the process of separation from their parents [1,2]. Preoperative anxiety has been reported to result in adverse outcomes and negative postoperative sequelae such as emotional disturbance, cognitive disturbance, behavioral problems, bad dreams, sleep disturbance, and disobedience [3]. To reduce children’s anxiety, it has been suggested that the parents move together with their children to the operating room or sedative agents should be provided [4].

However, moving to the operating room with parents has some problems. First, parents must be educated to prevent operating room contamination. Second, parents should not appear anxious to avoid influencing their children’s anxiety [5]. Third, parents should also wear surgical suits, which may be not effective in reducing children’s anxiety. The use of sedative drugs can be an effective way to reduce children’s anxiety, but it is difficult to
determine the effective dosage because children have a narrow safety margin and a large variation among sedative drugs [6]. Thus, several studies have been conducted to reduce anxiety in children by nonpharmacological methods. Numerous nonpharmacological methods have been investigated, including music [7], clowns [8], toys, comic books [9], and watching videos using smartphones or tablets [10]. Some of these strategies have been reported to reduce preoperative anxiety, with effects equivalent to or better than parental presence or sedative drugs.

Traditional pharmacological and nonpharmacological methods have their own pros and cons. Their effectiveness also depends on the children's characteristics or hospital conditions. Generally, a patient scheduled to undergo an operation is transferred using a stretcher car, which may be stressful for the patient. Moreover, children may show severe anxiety because of the synergistic effect of separation from their parents. In 1988, it was reported that the use of a pleasant mode of transportation, such as a little red wagon, could keep children calm and distracted during transport to the operating room [11], and this method has been introduced in literatures as a nonpharmacological anxiolytic intervention for children. Until recently, however, this simple method has not been evaluated through clinical trials. Only a very recent study by Liu et al. [12] compared the anxiolytic effect of transport in a children's toy car to that in a conventional transport vehicle, and favorable results were obtained in children aged 2–5 years. However, there is still limited evidence to support the effect of the transport method on reducing preoperative anxiety among children, and furthermore, it is not clear whether this anxiolytic effect varies according to the age of the children.

The primary goal of this study was to evaluate the effect of a wagon as a transport vehicle instead of the standard stretcher car to reduce children's anxiety related to separation from their parents. The secondary goal was to evaluate whether this anxiolytic effect was related to age.

Materials and Methods

The study population consisted of 80 children aged 2–7 years, classified as American Society of Anesthesiologists physical status I and scheduled for elective surgery under general anesthesia. After receiving approval by the Institutional Review Board of our hospital (CNUH-2016-185) and registration at clinicaltrials.gov (NCT03018145), the parents of all the children provided informed consent. Children with a history of anesthesia or surgery, with developmental delay, weighing over 34 kg, with severe pain, or who were administered psychotomimetic drugs within 24 h were excluded. From January to April 2017, 80 children scheduled for elective surgery were randomly allocated into one of two groups using a computer-generated method on the day of surgery: one group used a standard transport stretcher (Stryker®; Stryker Medical, USA; Fig. 1A) as a transportation method from the preoperative waiting area to the operating room (stretcher group, n = 40); the other group used a wagon (All Around Canopy Wagon™; Step2, USA; Fig. 1B) instead of a standard stretcher car (wagon group, n = 40). For analysis concerning the age of the children, we allocated the same number of children to the stretcher and wagon groups by computer-generated randomization with a block size of four with stratification for age (2–4 years or 5–7 years).

Each child was evaluated three times by the same anesthesiologist: before separation from his/her parents in the preoperative waiting area (T0), after separation from his/her parents in the hallway of the waiting area to the operating room, immediately before entry into the operating room (T1), and in the operating room before the induction of general anesthesia (T2). An anesthesiologist used the Modified Yale Preoperative Anxiety Scale (mYPAS) to assess the child's anxiety in five domains of behavior: activity, emotional expression, state of arousal, vocalization, and the presence of a parent [13]. In this method, each domain is rat-
ed from 1 to 4 except for the vocalization domain, which is rated from 1 to 6, with higher scores indicating a greater level of anxiety. The total mYPAS score was calculated by dividing each domain's rating by its highest possible rating. Parents were not allowed to enter the operating room, and so accompanied the child only in the preoperative waiting area. After separation from the parents, the interaction with the parents was assessed by slightly modifying the original components of the ‘use of parent’ because of parental absence.

Before the surgery, each child answered the EAS questionnaire (The Emotionality, Activity, and Sociability Temperament Survey for Children: Parental Ratings) to evaluate the child’s activity and sociability temperament. All children had a fasting time of over 6 h and did not take any premedication. After arrival at the preoperative waiting area with parents, the children’s mYPAS scores were assessed by an anesthesiologist (T0). The children were moved to the transport vehicle and then allowed to stay with parents for 2–3 min to adapt to the vehicle. After separation from the parents, the children were transferred to the assigned operating room through the hallway with the anesthesiologist, surgeon, and nurse for safety. At the end of the hallway, the anesthesiologist assessed the mYPAS scores before entry into the operating room (T1). In the operating room, the children were moved to the operating table for general anesthesia, and then the anesthesiologist assessed the mYPAS score again (T2).

**Statistical analysis**

The sample size calculation for the present study was based on the difference in the mYPAS after separation from the parents (T0 to T1). According to the results of a pilot study (n = 8 in each group, total n = 16), the mean difference was 10 and the standard deviation was 15 in each group (effect size = 0.6666667). With an estimated sample size for 80% power with a set α of 0.05 for the Student’s t test, a total sample size of 74 was calculated (n = 37 per group). We assigned 40 children per group to account for potential dropout. All statistical analyses were performed using statistical software (IBM SPSS Statistics version 20; IBM Corp., USA). Continuous variables were verified for normal distribution using the Kolmogorov-Smirnov test. The children’s age, weight, and EAS score were analyzed using an independent t test, and the results are presented as the mean ± SD. Differences in the mYPAS scores between groups at each time point were analyzed using the non-parametric Mann-Whitney test and are presented as the medians (1Q, 3Q). Within-group mYPAS changes were analyzed using Wilcoxon’s signed-rank test. Categorical data were analyzed using Pearson’s chi-square test. The relationships of children’s ages to mYPAS scores or mYPAS score changes were analyzed by Spearman correlation analysis. A P value < 0.05 was deemed to indicate statistical significance.

**Results**

The final data were collected from 76 children: 39 forming the conventional standard group (Stretcher group), and 37 forming the intervention group (Wagon group). Two children refused to ride the wagon or stretcher car, and two children took sedative premedication (Fig. 2.).

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**Fig. 2.** CONSORT flow chart showing the flow of patients through the trial.

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There were no significant differences in demographic variables or EAS questionnaire ratings between the groups, and there was no correlation between the EAS rating and mYPAS score (Table 1).

In the preoperative waiting area (T0), both groups showed similar mYPAS scores. In the Stretcher group, there was a significant increase in mYPAS during transportation after separation from parents (T1–T0, P = 0.001) and before induction of anesthesia (T2–T0, P = 0.003) compared with that in the waiting area (T0). The mYPAS score was significantly lower in the Wagon group during transportation than in the Stretcher group (T1, P = 0.007). However, use of the wagon did not prevent an increase in mYPAS scores before induction of anesthesia (Table 2).

Fifty-eight children (31 in the Stretcher group and 27 in the Wagon group) showed baseline anxiety (mYPAS scores > 30). The percentage of children with an increase in mYPAS from baseline was significantly higher in the Stretcher group than the Wagon group (Table 2).

Children’s age was weakly related to the baseline mYPAS score, with the baseline anxiety level tending to be lower with increasing age (r = −0.248, P = 0.031). During transportation to the operating room, relative increases in the mYPAS score from baseline (T1–T0) were negatively correlated with the age of children in the Stretcher group (r = −0.340, P = 0.034), indicating that younger children tended to be more anxious in the Stretcher group. However, no such correlation was observed in the Wagon group (r = −0.053, P = 0.756) (Fig. 3).

Subsequently, the mYPAS scores were compared between children aged 2–4 years and 5–7 years according to the transport method. In younger children (2–4 years), the mYPAS scores at T1 were significantly lower in the Wagon group (50.0 [23.3, 68.3]; n = 19) compared with the Stretcher group (83.3 [36.7, 95.0]; n = 19) (P = 0.018), and the mYPAS scores at T2 were also significantly lower in the Wagon group (46.7 [23.3, 53.3]) compared with the Stretcher group (73.3 [46.7, 96.7]) (P = 0.017). In older children (5–7 years), the mYPAS scores at T1 was lower in the Wagon group (28.3 [26.7, 37.9]; n = 18) than in the Stretcher group (50.0 [29.2, 55.0]; n = 20) (weak significance, P = 0.046), and the mYPAS scores at T2 were similar in both groups (44.1 [35.8, 55.4] in the Wagon group vs. 45.8 [36.7, 58.2] in the Stretcher group, P = 0.851).

Discussion

In the present study, we measured children’s anxiety using the mYPAS, ranging from 23.33 to 100. It is well known that mYPAS has strong interrater reliability [14]. A cutoff value of 30 is regarded as anxiety. In the present study, 76% of children showed anxiety (mYPAS > 30) even though they were with their parents.

Table 1. Children’s Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Stretcher group (n = 39)</th>
<th>Wagon group (n = 37)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>4.3 ± 1.4</td>
<td>4.3 ± 1.5</td>
<td>0.942</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>18/21</td>
<td>18/19</td>
<td>0.828</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>18.9 ± 5.3</td>
<td>18.8 ± 5.1</td>
<td>0.671</td>
</tr>
<tr>
<td>EAS score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotionality</td>
<td>13.7 ± 2.9</td>
<td>14.1 ± 3.8</td>
<td>0.667</td>
</tr>
<tr>
<td>Activity</td>
<td>18.6 ± 3.4</td>
<td>19.4 ± 3.6</td>
<td>0.397</td>
</tr>
<tr>
<td>Sociability</td>
<td>34.5 ± 4.8</td>
<td>35.3 ± 5.5</td>
<td>0.593</td>
</tr>
<tr>
<td>Type of surgery, n (%)</td>
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<td></td>
<td>0.917</td>
</tr>
<tr>
<td>Eye surgery</td>
<td>23 (59.0)</td>
<td>19 (51.4)</td>
<td></td>
</tr>
<tr>
<td>ENT surgery</td>
<td>6 (15.4)</td>
<td>6 (16.2)</td>
<td></td>
</tr>
<tr>
<td>Herniorrhaphy</td>
<td>5 (12.8)</td>
<td>6 (16.2)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>5 (12.8)</td>
<td>6 (16.2)</td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD or number of patients (%). EAS: Emotionality, Activity, and Sociability-Temperament Survey for Children-Parental Ratings; ENT: Ear, nose, and throat.

Table 2. Anxiety Level (mYPAS Scores) and Proportion of Changes in Anxiety

<table>
<thead>
<tr>
<th></th>
<th>Stretcher group (n = 39)</th>
<th>Wagon group (n = 37)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mYPAS scores</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>T0</td>
<td>46.7 (31.7, 65.0)</td>
<td>46.7 (28.3, 55.0)</td>
<td>0.332</td>
</tr>
<tr>
<td>T1</td>
<td>51.7 (36.7, 83.3)*</td>
<td>36.7 (26.7, 51.7)†</td>
<td>0.007</td>
</tr>
<tr>
<td>T2</td>
<td>51.7 (36.7, 75.0)*</td>
<td>46.7 (32.5, 54.2)</td>
<td>0.057</td>
</tr>
<tr>
<td>Proportion of children [n (%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline mYPAS score &gt; 30 at T0</td>
<td>31 (79%)</td>
<td>27 (73%)</td>
<td>0.354</td>
</tr>
<tr>
<td>Increase in mYPAS score at T1</td>
<td>23 (59%)</td>
<td>12 (27%)</td>
<td>0.020</td>
</tr>
<tr>
<td>Increase in mYPAS score at T2</td>
<td>22 (56%)</td>
<td>12 (27%)</td>
<td>0.036</td>
</tr>
</tbody>
</table>

Values are presented as median (IQR) or number of parents (%). mYPAS: Modified Yale Preoperative Anxiety Scale. T0: in the waiting area with parents, T1: on the transporting vehicle after separation from patients, T2: before anesthesia induction. *P < 0.05 compared with T0 within the group by Wilcoxon signed-rank test, †P < 0.05 compared with the Stretcher group by Mann-Whitney test, ‡P < 0.05 compared with Stretcher group by Pearson chi-square test.

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These results are comparable with those of a previous study that reported 80.5% of children had anxiety [15]. In that study, more than 60% of children showed an increase in mYPAS score after separation from their parents. This result was similar to ours in the Stretcher group (59%).

In the Wagon group, the median mYPAS score of 36.7 after separation from their parents was similar to that in another study (33.4) in which children came into the operating room together with their parents [16]. In addition, the proportion of children with increased anxiety compared to baseline was significantly lower in the Wagon group until induction of anesthesia. These results suggest that the wagon can play a role in the management of preoperative anxiety in children, comparable to other non-pharmacological methods such as parental presence or video distraction [16].

The anxiety-reducing effect of the wagon may be related to its greater familiarity to children compared to the stretcher car, and it may distract the children similar to watching a video or playing with toys. It also feels like going on a ride and will be fun for children. In addition, children mostly lie down in the stretcher car to reduce the risk of falling, but they can sit up in the wagon, and so children can freely see their surroundings and feel less restrained.

In general, one of the most commonly used methods to reduce children’s anxiety is oral or parenteral sedative medication [4,17,18]. However, sedative drugs sometimes have several undesirable effects, including respiratory depression, hypotension, seizure-like activity, and paradoxical reactions [18,19]. Moreover, it is difficult to determine the effective dosage because children have a narrow safety margin and a large variation among sedative drugs [6]. According to previous studies, a combined therapy with nonpharmacological and pharmacological interventions was more effective than medication alone [8,10]. The wagon as a transport vehicle can be used in combination with conventional pharmacological and nonpharmacological methods.

Previous studies showed that younger children have more anxiety than older children [20,21]. We allocated children to both younger and older groups for analysis related to the children’s ages. According to our protocol, we included children aged between 2 and 7 years; because the median age was 5 years, we divided the children into a younger subgroup aged 2.0–4.9 years and an older subgroup aged 5.0–7.9 years. In our study population (2.0–7.9 years), younger children showed greater baseline anxiety than older children, as shown in previous studies [8,20]. This result suggests that older children are more likely to endure or overcome stress than younger children.

In the present study, change in anxiety after separation from parents decreased as the children’s age increased in the Stretcher group. The intensity of separation anxiety is known to peak at around one year of age, and then declines with age, largely because of increasing cognitive abilities [22]. Therefore, the intensity of separation anxiety in younger children is usually higher than that in older children. In the Wagon group, however, children’s
age was not related to change in anxiety. These results suggest that use of the wagon may have offset the increase in anxiety in younger children that was observed in the Stretcher group. Thus, use of the wagon may be expected to be more effective in younger children than in older children.

However, before induction of anesthesia (T2), the wagon did not prevent increases in the mYPAS score, although the proportion of children in whom the mYPAS score increased at baseline (T0) was lower in the Wagon group than in the Stretcher group. This may have been because preoperative anxiety in older children often originates from the fear of surgery rather than the distress of separation [10]. Similarly, Kain et al. [23] suggested that interactive music therapy may be useful in alleviating preoperative anxiety due to separation from parents and entrance to the operating room; however, music therapy did not appear to alleviate children’s anxiety at induction of anesthesia.

A recent randomized controlled study demonstrated that riding in a toy car significantly reduced preoperative anxiety compared with riding on a stretcher among children with or without premedication, which was consistent with our results [12]. Interestingly, the anxiolytic effect of riding in a toy car was similar to that of oral midazolam, even just before anesthesia induction in the previous study [12]. These favorable results may have been due to the age range of the study population (2–5 years), which corresponds to the younger children in the present study. As suggested above, the anxiolytic effect of the transport method may be affected by the children’s age, and it would have a greater effect in younger children.

The present study had several limitations. First, our results showed higher baseline mYPAS scores than those reported in previous studies [15,16]. This may have been due to the lack of sedative premedications, which were administered in other studies. Here, we wanted to eliminate the effects of drugs. Similarly, another study in which children did not take premedication in the waiting area showed a higher mYPAS score [10]. Second, blinding was impossible in this study because the transportation vehicles were visible to the investigators, and therefore observer bias may have influenced assessment of anxiety levels. Third, we were unable to calculate the ‘use of parents’ item of the mYPAS accurately at the T2 time point because of parental absence. Therefore, the components of the use of parent may have affected the psychometric integrity of the mYPAS.

In summary, most children scheduled for surgery showed anxiety during transportation to the operating room and before the induction of anesthesia. Younger children showed more anxiety than older children. The wagon as a transport method decreased this anxiety compared with the standard stretcher car. This result suggests that wagons may be a good alternative to reduce children’s preoperative anxiety. In addition, the wagon also has a number of advantages: it is a very simple change in transportation and can be used in combination with pharmacological or other nonpharmacological methods.

**Conflicts of Interest**

No potential conflict of interest relevant to this article was reported.

**Author Contributions**

Sun-Hong Park (Data curation; Investigation; Writing – original draft; Writing – review & editing)
Sanghee Park (Data curation; Formal analysis; Writing – review & editing)
Seongheon Lee (Conceptualization; Formal analysis; Writing – review & editing)
Jeong Il Choi (Methodology; Supervision; Writing – review & editing)
Hong-Beom Bae (Methodology; Supervision; Writing – review & editing)
Youngwook You (Data curation; Investigation; Writing – review & editing)
Seongtae Jeong (Conceptualization; Formal analysis; Methodology; Writing – original draft; Writing – review & editing)

**ORCID**

Sun-Hong Park, https://orcid.org/0000-0002-0566-9067
Sanghee Park, https://orcid.org/0000-0003-3743-4024
Seongheon Lee, https://orcid.org/0000-0002-2675-2521
Jeong Il Choi, https://orcid.org/0000-0002-3571-2599
Hong-Beom Bae, https://orcid.org/0000-0002-0358-6807
Youngwook You, https://orcid.org/0000-0003-3599-0246
Seongtae Jeong, https://orcid.org/0000-0002-6245-9779

**References**

The effect of the type of anesthesia on the quality of postoperative recovery after orthopedic forearm surgery

A Ram Doo¹,², Sehrin Kang¹, Ye Sull Kim¹, Tae-Won Lee¹, Jun-Rae Lee¹,², Dong-Chan Kim¹,²

¹Department of Anesthesiology and Pain Medicine, Jeonbuk National University Hospital, ²Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, Jeonju, Korea

Background: Although the quality of postoperative recovery may be affected by factors, there are few investigations whether the type of anesthesia also affects it. In this single-blinded, prospective, observational study, we compared the quality of postoperative recovery in patients undergoing orthopedic forearm surgery under general or regional anesthesia (brachial plexus block).

Methods: Ninety-seven subjects, aged 18–65 years and American Society of Anesthesiologists physical status I or II, undergoing orthopedic forearm surgery, were allocated to general or regional anesthesia group. The quality of postoperative recovery was assessed using a validated Korean version of Quality of Recovery-40 (QoR-40K) questionnaire. Patients were surveyed three times, the day before surgery (baseline) and 1st and 7th day after the surgery, and the scores of both groups were compared.

Results: We analyzed 47 and 50 patients in general and regional anesthesia, respectively. The global QoR-40K score and those of each of its five dimensions were not significantly different between the two groups at baseline, 1st and 7th day postoperatively. In two-way RM ANOVA, the global QoR-40K score at postoperative 1st day was significantly lower than that of baseline (P < 0.001) and postoperative 7th day (P < 0.001), respectively, in both general and regional anesthesia groups. However, there was no significant difference at each timepoint between the two groups.

Conclusions: The present study suggests that brachial plexus block with intravenous dexmedetomidine infusion does not improve the quality of postoperative recovery compared to sevoflurane inhalation anesthesia with remifentanil infusion in patients undergoing orthopedic forearm surgery.

Keywords: General anesthesia; General surgery; Orthopedic surgery; Postoperative recovery; Quality; Regional anesthesia.

Introduction

Postoperative recovery is one of the major concerns for patients undergoing surgery. Most patients expect fast recovery of function following anesthesia and surgery, but in some instances, delayed postoperative recovery may cause a patient discomfort, a longer hospital stay, a delayed return-to-work, and increased health care costs. In the past, postoperative morbidity or mortality had been the major concerns associated with postoperative recovery outcomes. However, consistent with the current trends in the advanced health care system, the concept of patient-centered care has emerged as the primary approach for improving quality and safety of medical care services. In this context, patient-focused quality of postoperative recovery has been recognized as one of the most...
important considerations in perioperative medicine.

Although the quality of postoperative recovery may be affected by several factors, such as the choice of anesthetic drugs [1,2], administration of a nerve block for postoperative analgesia [3–5], or several multimodal anesthetic or analgesic medications or interventions [6–9], there are few studies that have investigated whether the type of anesthesia (general vs. regional anesthesia) used affects the quality of postoperative recovery. The brachial plexus block is the most commonly used regional anesthesia method for upper extremity surgeries. The benefits of brachial plexus block are well known to reduce postoperative pain and opioid consumption and to improve intraoperative hemodynamic stability and patient satisfaction [10,11]. However, it is unknown whether a brachial plexus block positively affects the patient-focused quality of postoperative recovery or not.

In the present study, we hypothesized that the quality of postoperative recovery in patients undergoing orthopedic forearm surgeries would be better with brachial plexus block than with general anesthesia.

Materials and Methods

This study was approved by the Institutional Review Board of Chonbuk National University Hospital (CUH 2017-09-005) and registered at WHO International Clinical Trials Registry Platform (KCT0003503). After obtaining the written informed consent, 119 patients, aged 18–65 years and American Society of Anesthesiologists physical status I or II, who were undergoing orthopedic forearm surgeries during the period between November 2017 and April 2019 were enrolled in this single-blinded, prospective, observational study. Patients with a literacy problem, language difficulties, a history of psychotic disorder, allergic reactions to local anesthetics, or coagulation abnormalities were excluded from this study. The subjects were allocated to either the general or regional anesthesia group per anesthesiologist’s decision based on each patient’s medical condition and their preferred anesthesia method without randomization. The anesthetic regimen was standardized for both the general and regional anesthesia groups. On arrival in the operating room, standard anesthetic monitoring including electrocardiogram, pulse oximetry, and noninvasive blood pressure was employed in all subjects regardless of the allocated group. In addition, in the general anesthesia group, bispectral index (BIS) monitoring was employed in order to optimize the depth of anesthesia.

General anesthesia was induced with 1.5–2.5 mg/kg of propofol and 0.3–0.8 mg/kg of rocuronium, and effect-site concentration of 1–3 ng/ml remifentanil was infused using a target-controlled infusion pump (Orchestra® Base Primea, Fresenius Vial, France). Anesthesia was maintained with sevoflurane 1–4 vol% in 50% oxygen and remifentanil 1–3 ng/ml in order to maintain non-invasive arterial pressure and heart rate within preanesthetic values. i-gel (i-gel™; Intersurgical Ltd., UK) or endotracheal tube was used for securing the airway during surgery. End-tidal carbon dioxide partial pressure and BIS value were maintained at 30–35 mmHg and 40–65, respectively. Once the surgery was completed, the administration of the anesthetics was stopped, and a residual neuromuscular block was antagonized with neostigmine 50 μg/kg and glycopyrrolate 10 μg/kg at the appearance of the second twitch response (T2) during the train-of-four count.

In the regional anesthesia group, the patients were premedicated with midazolam 1–2 mg intravenously. After the usual sterile preparation, the patients were scanned with a 13–6 MHz linear array transducer (EDGE® ultrasound machine, Sonosite Inc., USA) in order to identify the brachial plexus lying anterolateral to the subclavian artery in the supraclavicular fossa. Under the guidance of real-time ultrasonography, a 25-gauge, 5 cm short-bevel needle was inserted toward the brachial plexus using an in-plane technique and a lateral to medical direction. In the current study, as has been described in previous studies, half the volume of lidocaine 1.5% with epinephrine 5 μg/ml (16 ml) was injected into the main neural cluster, following which, the remaining half (16 ml) was injected into every single satellite neural cluster for a targeted intrachannel injection [12,13]. All procedures were performed by a single skilled anesthesiologist (Dr. A.R. Doo) with experience of regional anesthesia for more than 5 years.

Subsequently, the extent of sensory blockade was evaluated via a pinprick test along the musculocutaneous, median, radial, and ulnar distribution every 5 min intervals until a successful blockade was confirmed, which was defined as complete loss of pinprick sensation. After successful blockade was confirmed, an intravenous dexmedetomidine infusion was started (loading 1 μg/kg over 10 min followed by 0.2–0.6 μg/kg/h), and 3 L/min of oxygen was supplied via a nasal cannula. During the operation, the target Modified Observer’s Assessment of Alertness/Sedation scale (MOAA/S) 3–4, which presented moderate sedation, was maintained by titrating the dose of infusion (MOAA/S, 5 = responds readily to name spoken in normal tone, 4 = lethargic response to name spoken in normal tone, 3 = responds only after name is called loudly or repeatedly, 2 = responds only after mild prodding or shaking, 1 = responds only after painful trapezius squeeze, 0 = no response after painful trapezius squeeze).

In both groups, the hemodynamic parameters including the noninvasive blood pressure, heart rate, and peripheral oxygen saturation were recorded until the end of the surgery. The adverse
events including bradycardia (heart rate < 50 bpm) and hypotension (systolic blood pressure < 90 mmHg or a decrease more than 30% of baseline value) were recorded and treated with intravenous atropine 0.5 mg and ephedrine 5–10 mg, respectively. All the patients routinely received ketorolac 30 mg and nefopam 20 mg intravenously during the skin closure for postoperative pain management. During postoperative recovery in the postanesthesia care unit (PACU), pain (Numeric rating scale [NRS] ≥ 4 using 11-point scale, 0 = no pain, 10 = worst pain imaginable) was treated with fentanyl 1 μg/kg increments every 5 min. The NRS score, total fentanyl consumption, and development of postoperative nausea and vomiting (PONV) were recorded. The patients were discharged to the ward when the modified Aldrete score was 9 or more.

Assessment of quality of postoperative recovery

The quality of postoperative recovery was assessed using a validated Korean version of Quality of Recovery-40 (QoR-40K) questionnaire [14]. QoR-40K is composed of 40-items of five dimensions including emotional state, physical comfort, psychological support, physical independence and pain [14,15]. Each item is rated on a 5-point Likert scale (1 = none of the time, 2 = some of the time, 3 = usually, 4 = most of the time, 5 = all of the time), and the global score ranges from 40 to 200. The patients were surveyed at three timepoints, the day before the surgery (baseline), 24 h after the surgery, and 7 d after the surgery (after discharge). The primary outcomes were the QoR-40K results. At the 24-h timepoint after the surgery, the patients were asked to fill the QoR-40K questionnaire similar to during the baseline evaluation that was conducted in the patient’s ward. Meanwhile, on the 7th day after the surgery, QoR-40K was evaluated again via a telephone call between 4 and 6 pm by a single investigator, Dr. S.R. Kang who was blinded to the allocated groups.

Statistical analysis

The primary outcome was the global QoR-40K score evaluated on the 1st day postoperatively. For the two groups, a sample size of 51 subjects each was estimated to achieve 80% power to detect a 6.3-point difference in the QoR-40 score. A 6.3-point difference was identified by a previous study to be the minimal clinically important difference (MCID) in the QoR-40 score [16]. Considering the dropout rate of 20%, the sample size was enlarged to 123 patients. All the descriptive statistics are expressed as mean ± standard deviation (SD), median (25th–75th percentile), percentage or the number of patients. Continuous variables including QoR-40K scores were analyzed with Student’s t-test or Mann-Whitney rank-sum test after a normality test, and categorical variables including opioid usage and incidence of PONV were analyzed using Chi-square test.

The QoR-40K scores of both groups were analyzed with two-way repeated measures analysis of variance (RM ANOVA) with spherical test, and the Bonferroni t-test was used for post-hoc analysis. All statistical analyses were performed using SigmaPlot version 12.5. (Systat Software Inc., USA), and P values < 0.05 were considered statistically significant.

Results

The details of subject flow are shown in Fig. 1. Among the 119 patients who were enrolled, 97 patients (47 in the general anesthesia group and 50 in the regional anesthesia group) completed the study, and their results were analyzed. Among the 22 patients excluded from the study in both group, two patients were excluded due to the incomplete motor and sensory block in the regional anesthesia group. Patients’ demographics and clinical characteristics were not different between the two groups except anesthesia maintenance time (Table 1). Although there was no significant difference in both surgery time and anesthesia induction time between the two groups, the anesthesia maintenance time was significantly longer in the general anesthesia group compared to that in the regional anesthesia group (P = 0.019).

Postoperative quality of recovery was not significantly different between two groups. The global QoR-40K scores and each score of the five dimensions were not significantly different between the two groups at preoperative, postoperative 1st and 7th day (Table 2). In two-way RM ANOVA and Bonferroni post-hoc analysis, global QoR-40K score on the postoperative 1st day was significantly lower than that of preoperative baseline (P < 0.001) and postoperative 7th day (P < 0.001), respectively, in both general and regional anesthesia groups. However, there was no significant difference at each timepoint between the two groups (Fig. 2).

The regional anesthesia group exhibited better recovery profile in the PACU than the general anesthesia group (Table 3). Pain score and opioid consumption in the PACU were lower in the regional anesthesia group than in the general anesthesia group, respectively (P < 0.001 and P < 0.001). Additionally, the incidence of PONV was 10.6% in the general anesthesia group while none of the patients experienced PONV in the regional anesthesia group in PACU (P = 0.024). The duration of PACU stay was significantly shorter in the regional anesthesia group than in the general anesthesia group (P = 0.018).

The hemodynamic parameters including mean arterial pres-
Table 1. Patient Demographics and Clinical Characteristics

<table>
<thead>
<tr>
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<th>General group (n = 47)</th>
<th>Regional group (n = 50)</th>
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</tr>
</thead>
<tbody>
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<td>Sex (M/F)</td>
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<td>29/21</td>
<td>0.951</td>
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<tr>
<td>ASA PS (I/II)</td>
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<td>39/11</td>
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<td>Age (yr)</td>
<td>44.0 (32.0–54.0)</td>
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<td>BMI (kg/m²)</td>
<td>24.8 ± 4.2</td>
<td>24.2 ± 3.6</td>
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<tr>
<td>Surgery time (min)</td>
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<td>35.0 (24.5–61.3)</td>
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<td>Anesthesia maintenance time (min)</td>
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<td>65.0 (50.0–100.0)</td>
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<td>Anesthesia induction time (min)</td>
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<tr>
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<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Carpal tunnel release</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Mass excision</td>
<td>5</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Surgical side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dominant/non–dominant arm</td>
<td>28/19</td>
<td>30/20</td>
<td>0.869</td>
</tr>
<tr>
<td>Duration of hospital stay (days)</td>
<td>6.0 (5.0–8.0)</td>
<td>6.0 (5.0–8.0)</td>
<td>0.437</td>
</tr>
</tbody>
</table>

Values are presented as number of patients, mean ± SD or median (25th–75th percentile). ASA PS: American society of anesthesiology physical status; BMI: body mass index. Anesthesia maintenance time: time elapsed from the beginning to the end of anesthesia. Anesthesia induction time: time elapsed from the beginning of anesthesia induction to the beginning of the surgery.
sures and heart rates were remained stable during the operation and PACU stay although there were significant differences between two groups at certain timepoints of measurement. Mean arterial pressures and heart rates were significantly lower in the general anesthesia group compared to the regional anesthesia group at skin incision and 10 min after skin incision, respectively. And mean arterial pressures were significantly lower in the regional anesthesia group compared to the general anesthesia group at PACU admission and 30 min after PACU admission. However, in both group, there were no incidence of hypotension or bradycardia during the operation and PACU stay (Fig. 3).

Discussion

The results of the present study suggest that the type of anesthesia (general vs. regional anesthesia) does not affect patient-focused quality of postoperative recovery in patients undergoing orthopedic forearm surgery. Generally, postoperative recovery involves an initial abrupt decline in function followed by progressive recovery toward the preoperative state or to a new equilibrium state. The time period required for complete postoperative recovery is extremely diverse and depends on the type of surgery, surgical invasiveness, patient's medical condition, and other factors.
Although patient-focused quality of postoperative recovery is a complex outcome involving physiological, physical, functional, emotive, and nociceptive aspects, the authors assumed that the postoperative pain could potentially be the most important aspect involved in all of them during the early recovery stage. Several authors have reported that regional anesthesia provides significant benefits during the early recovery stage corresponding to the pain score, opioid consumption, opioid-related adverse effects, and length of hospital stay in comparison with general anesthesia [11,17]. Based on this, the authors hypothesized that patient-focused quality of postoperative recovery in patients undergoing orthopedic forearm surgery would be better with regional anesthesia than general anesthesia in the present study. However, the QoR-40K score was comparable between the general and regional anesthesia group during both the early recovery stage (postoperative 1st day) and late recovery stage (postoperative 7th day), even though the recovery profile including the pain score, opioid consumption and opioid-related complications in the PACU in the regional anesthesia group was superior to that in the general anesthesia group. To the best of our knowledge, this is the first investigation that evaluates the effect of the type of anesthesia on patient-focused quality of postoperative recovery in patients undergoing orthopedic forearm surgery.

There has been a concept of enhancing the quality of medical care such as quality improvement program and Joint Commission International standards [18]. Traditionally, the quality of medical care has been based on providers-focused outcomes such as the survival rate, surgical mortality, or cost-effectiveness. However, patient-centered and patient-reported quality of medical care service has been a recent focus. For instance, the QoR-40 is a widely-used, patient-centered, self-rated questionnaire for assessing a patient’s health status postoperatively, and several versions of this questionnaire in different languages have been validated [15,19–21]. QoR-40K, especially, has recently been demonstrated to be a valid, reliable and feasible tool that is used to evaluate Korean surgical patients [14]. QoR-40 is composed of 40-items of five di-

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**Table 3. Recovery Profile in Postanesthesia Care Unit**

<table>
<thead>
<tr>
<th></th>
<th>General group (n = 47)</th>
<th>Regional group (n = 50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain score (NRS; 0–10)</td>
<td>3 (2–4)</td>
<td>0 (0–0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Opioid usage [n (%)]</td>
<td>14 (29.8)</td>
<td>0 (0)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Cumulative fentanyl consumption (μg)</td>
<td>0 (0–52)</td>
<td>0 (0–0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>PONV [n (%)]</td>
<td>5 (10.6)</td>
<td>0 (0)</td>
<td>0.024††</td>
</tr>
<tr>
<td>Duration of PACU stay (min)</td>
<td>65.0 (60.0–90.0)</td>
<td>60.0 (50.0–70.0)</td>
<td>0.018*</td>
</tr>
</tbody>
</table>

NRS: numeric rating scale, n: number of patients, PONV: postoperative nausea and vomiting, PACU: postanesthesia care unit. *by Rank-sum test, †by Chi-square test, ††by Fisher's exact test.

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**Fig. 3. Hemodynamic parameters during surgery and in PACU. (A) Mean arterial pressures, (B) Heart rates.**

*There were significant differences in mean arterial pressures and heart rates between two groups by two-way RM ANOVA and Bonferroni posthoc analysis. bpm: beats per minutes, Pre-AN: pre-anesthesia, SI: skin incision, SI-10: 10 minutes after skin incision, SI-30: 30 minutes after skin incision, SI-60: 60 minutes after skin incision, SC: skin closure, PACU: postanesthesia care unit admission, PACU-30: 30 minutes after PACU admission.

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https://doi.org/10.4097/kja.19352
mensions including emotional state, physical comfort, psychological support, physical independence and pain. All the items are scored on a 5-point Likert scale, and consequently, the global score ranges from 40 to 200. Among the five dimensions, the items corresponding to physical independence may be influenced by the surgery of the dominant arm, because the inquiries include the ability to perform usual home activities such as brushing teeth or writing. Therefore, in the current study, we investigated whether the surgery was performed on the dominant forearm or not (Table 1).

Several studies including the current study simply compare the means of QoR-40 scores between the two groups [1–3]. However, a consensus on a statistical-analytical method that can be employed to assess a patient’s recovery after surgery using QoR-40 scores has not been well established. Several statistical methods such as distribution-based statistics of an individual’s change score or evaluation using predetermined threshold value or an estimated MCID has been recommended [16]. Furthermore, the timing of the recovery assessment differs amongst researches or tools. Most of the studies that assessed the QoR-40 scores limited their assessment to 24 h after the surgery. In the current study, in addition to assessing the QoR-40K scores at this timepoint, the authors assessed them at the one week timepoint after the surgery (after discharge) via telephone call in order to evaluate the restoration of functional activities in a daily living environment. Future studies should focus on the development of an accurate, reliable and valid methodology to assess postoperative recovery via the QoR-40 scoring system.

Meanwhile, one of the major concerns associated with regional anesthesia is how to shorten the duration of time that is required to perform the blocks while providing profound anesthesia and analgesia during surgery. As is well known, the application of ultrasound during a peripheral nerve block reduces the minimum effective analgesic volume, shortens the onset time, and increases the rate of successful blocks [22]. When compared with the axillary block, the supraclavicular approach has distinct advantages including faster onset, clear and simple sonoanatomy, and profound sensory and motor block with a lower volume of the local anesthetics via a single injection [12,23]. Furthermore, the ultrasound-guided targeted intracluster-injection method that was used in the current study has been reported to result in a quicker onset than other injection methods, such as the traditional corner pocket approach [13,24]. For these reasons, anesthesia induction time was not significantly different between the general and regional anesthesia groups in the present study.

Dexmedetomidine, a highly selective alpha-2 agonist, manifest sedative, sympatholytic, amnestic and analgesic properties. In our standard clinical practice, dexmedetomidine is routinely administered intravenously for sedation during surgery under regional anesthesia, because it provides a reliable and predictable level of sedation and better analgesia without respiratory complications. Moreover, the efficacy of dexmedetomidine in regional anesthesia is well established that improves the quality of regional anesthesia and prolongs the duration of analgesia when administrated either intravenously or perineurally. Lidocaine, which was used in the present study, is a frequently used local anesthetic drug for regional anesthesia practice because of its rapid onset of anesthesia and its safety; however, its limitation is a short duration of anesthesia.

In the current study, even though the duration of postoperative analgesia was not evaluated, prolonged analgesia was expected due to the application of brachial plexus block and the additional administration of dexmedetomidine in the regional anesthesia group. Nevertheless, better recovery profile in PACU including lower pain score, reduced opioid consumption and lower incidence of PONV in the regional anesthesia group did not positively affect the quality of postoperative recovery during the early postoperative recovery phase when compared to in the general anesthesia group.

There are study limitations. First, the present study was a prospective observational study without randomization. The authors assumed that patient-focused quality of recovery could be heavily influenced by the patient’s expectation or a previous experience associated with anesthesia. For example, if the patient received general anesthesia despite a strong preference for regional anesthesia, the patient satisfaction and patient-focused quality of recovery may be diminished. Second, as mentioned above, although lidocaine that was used in the present study is safe and brings on rapid onset of anesthesia, it yields a short duration of anesthesia. The use of long acting local anesthetics, which manifest long duration of analgesia, may affect the quality of postoperative recovery. Third, surgery-related outcomes including complication rates were not investigated in the present study. The effect of type of anesthesia on the surgical outcomes is still controversial. The overall provider- and patient-focused postoperative recovery outcome would be investigated in the future study. Fourth, the current study is limited by too small sample size to detect a difference of each scores of the five dimensions as well as the global QoR-40K score in both groups.

In conclusion, brachial plexus block with intravenous dexmedetomidine infusion does not appear to improve patient-focused quality of postoperative recovery compared to sevoflurane inhalation anesthesia with remifentanil infusion in patients who are undergoing orthopedic forearm surgery.
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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

A Ram Doo (Writing – original draft)
Sehrin Kang (Investigation)
Ye Sull Kim (Data curation)
Tae-Won Lee (Data curation)
Jun-Rae Lee (Supervision)
Dong-Chan Kim (Writing – review & editing)

ORCID

A Ram Doo, https://orcid.org/0000-0003-1310-790X
Sehrin Kang, https://orcid.org/0000-0001-8211-3831
Ye Sull Kim, https://orcid.org/0000-0001-8771-488X
Tae-Won Lee, https://orcid.org/0000-0002-3910-454X
Jun-Rae Lee, https://orcid.org/0000-0001-9619-2008
Dong-Chan Kim, https://orcid.org/0000-0001-6946-1129

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Combined supraclavicular and superficial cervical plexus block for clavicle surgery

Onur Baran¹, Bünyamin Kir¹, İrem Ateş¹, Ayhan Şahin², Ali Üztürk³

¹Clinic of Anesthesiology and Reanimation, Palandöken State Hospital, Erzurum, ²Department of Anesthesiology and Reanimation, Medical Faculty of Namik Kemal University, Tekirdağ, ³Clinic of Orthopedics and Traumatology, Palandöken State Hospital, Erzurum, Turkey

**Background:** Clavicle fractures occur in 35% of shoulder girdle fractures. Surgical fixation is preferred, especially in young patients for optimal functional outcomes, while nondisplaced fractures are usually treated conservatively.

**Case:** A 38-year-old male patient was admitted to the emergency services with a fracture of the left clavicle following a fall. During the preoperative evaluation, the patient requested to be awake during the surgery. Combined supraclavicular and superficial cervical plexus block was performed under ultrasound guidance without complications and the patient experienced no pain.

**Conclusions:** This technique may avoid possible complications related to interscalene brachial plexus block. Future studies are required to confirm the safety and efficacy of this approach.

**Keywords:** Clavicle; Nerve block; Ultrasonography.

Clavicle fractures occur in 35% of shoulder girdle fractures. While nondisplaced fractures are usually treated conservatively, surgical fixation is preferred especially in young patients for optimal functional outcomes [1]. Clavicular surgery can be performed under general or regional anesthesia with peripheral nerve blocks [2].

The supraclavicular nerves originate from the superficial cervical plexus and innervate the skin overlying the clavicle [1,3]. The superior trunk of the brachial plexus also includes the supraclavicular branches including the dorsal scapular nerve, the long thoracic nerve, the suprascapular nerves, and the nerve to the subclavius that arise superior to the clavicle [3]. Opinions vary regarding the innervation of the clavicle. Pain transmission may be mediated by the superficial cervical plexus or the subclavian nerve alone; however, the precise pathway is uncertain. The superficial cervical plexus block may be used alone or in combination with the deep cervical plexus block, interscalene brachial plexus block, or supraclavicular brachial plexus block for surgical anesthesia and postoperative analgesia for clavicle surgery [4]. When compared to the interscalene brachial plexus block, the supraclavicular brachial plexus block has lower rates of phrenic nerve palsy [5]. The supraclavicular brachial plexus block carries the risk of pneumothorax; however, it occurs only when the inferior divisions are blocked. A written informed consent was obtained from the patient prior to the procedure.

**Case Report**

A 38-year-old male patient was admitted to the emergency services after he had slipped and fallen on an icy footpath that resulted in a fracture of the left clavicle. A consultation
was requested from Department of Orthopedics and Traumatology. Following evaluation by the orthopedic surgeon, open surgery with internal fixation was planned. The patient had no previous history of surgery, drug usage, or allergy and had no co-morbidities. During the preoperative evaluation, the patient requested to be awake during the surgery. A peripheral nerve block was planned and the patient was offered detailed information regarding the procedure.

In the operating room, monitoring was established with electrocardiogram, SpO₂ measurement, and non-invasive blood pressure measurement. An intravenous infusion of 0.9% sodium chloride was commenced. Midazolam, 2 mg, was administered intravenously for sedation. The patient was placed in a semi Fowler’s position, head rotated to right 30 degrees. The left side of the neck was cleaned with povidone-iodine. The block site and the surface of the ultrasound probe were covered with a sterile dressing. A linear transducer was placed at the level of the thyroid cartilage at the posterior border of the sternocleidomastoid muscle. The carotid artery was identified on scanning the neck in an anteroposterior direction. Color Doppler was used to confirm the presence of other blood vessels at the site of the block. The probe was moved laterally after identification of the carotid artery and the posterior border of the sternocleidomastoid muscle was centered on the screen. Using an in-plane technique, the needle was inserted close to the lateral end of the probe from lateral to medial through the thyroid cartilage. The tip of the needle was tracked under ultrasound guidance and positioned in the fascia deep to the sternocleidomastoid muscle. The local anesthetic solution was administered after confirmation of the needle tip position and a negative aspiration test. A mixture of 10 ml of 0.5% bupivacaine and 5 ml of 2% lidocaine was injected into the superficial cervical fascia (Fig. 1).

We decided to perform a supraclavicular brachial plexus block to avoid the side effects of the interscalene approach. The probe was placed in the supraclavicular fossa parallel to the clavicle. In contrast to the classic approach to supraclavicular brachial plexus block, we aimed to block the divisions originating from the superior trunk alone. After identifying the pulsations of the carotid artery, we applied color Doppler for identification and confirmation of any other vascular structures at the site of needle insertion. The needle was inserted using an in-plane technique from lateral to medial. The needle was tracked under vision and advanced through the platysma muscle and the fascia covering the brachial plexus. After the needle had passed through the fascia, a mixture of 5 ml of 0.5% bupivacaine and 5 ml of 2% lidocaine was injected after a negative aspiration test. After confirmation of the absence of pain, surgery was commenced. The procedure lasted for nearly 2 hours during which there was no significant variation in heart rate or blood pressure and the patient did not experience any pain. No complications such as Horner’s syndrome or phrenic nerve palsy were observed during the procedure; no additional opioids or benzodiazepines were administered (Fig. 2).

Discussion

We prefer regional anesthesia techniques for clavicular surgery considering the difficult airway access in the sitting position intraoperatively and the likelihood of complications related to general anesthesia. In the present case, we decided to combine a block of the upper trunks of the brachial plexus with the superficial cervical plexus block to avoid the complications related to the interscalene brachial plexus block.
In a previous case report by Herring et al. [2], a 20-year-old patient presented to the emergency department with severe pain following a fall on the shoulder the previous day. A fracture of the clavicle was diagnosed on radiography. A superficial cervical plexus block was performed with 8 ml 0.5% bupivacaine under ultrasound guidance to alleviate the pain. The pain score reduced to 2/10 from 9/10 and the analgesic effect lasted for approximately 20 hours.

A superficial cervical plexus block may be effective for postoperative analgesia but it may not be adequate for intraoperative analgesia. Supplemental block with an interscalene or a supraclavicular brachial plexus block is required in most cases for adequate intraoperative analgesia. Contractor et al. [6], in a previous study, performed ultrasound-guided cervical plexus and interscalene brachial plexus block in thirty patients undergoing clavicular surgery. A mixture of 10–15 ml of 1.5% lignocaine with adrenaline and 5–10 ml of 0.5% bupivacaine was administered for interscalene brachial plexus block and 10 ml of 0.25% bupivacaine for the superficial cervical plexus block. All procedures were completed under regional anesthesia alone; however, Horner’s syndrome was observed in 8 patients (26.7%) and hoarseness of voice occurred in 5 patients (16.7%). Balaban et al. [4] reported 12 patients who underwent clavicle surgery under combined interscalene-intermediate cervical plexus block. They performed ultrasound-guided, single-insertion, double-injection block using an in-plane technique for intraoperative analgesia. All the procedures were completed solely under regional anesthesia. No early surgical or block-related complications were observed, suggesting that this technique may be an effective anesthetic technique for clavicle fixation. No acute complications were observed in this series; however, the small sample size may not confirm the safety of this approach.

Although traditional techniques may be used for clavicle fracture surgery, new approaches have been described. One of the recently described techniques is the new subclavian approach for selective supraclavicular nerve block under ultrasound-guidance. A 62-year-old woman with a left clavicular fracture, bilateral pneumothoraces, and severe renal dysfunction was scheduled to undergo open reduction and internal fixation. A selective supraclavicular brachial plexus block was performed to enable pain relief along the distribution of the supraclavicular nerve and the 5th and 6th cervical nerves and to avoid phrenic nerve palsy. Under ultrasound guidance using a high-frequency linear probe, 10 ml of 0.75% levobupivacaine was injected around C5 and C6. There was no spread of local anesthetic around the 4th, 5th, and 8th cervical nerves, thus avoiding phrenic nerve palsy that may have led to major complications in patients with bilateral pneumothoraces [7]. Similar concerns about the interscalene brachial plexus block were also raised by Reverdy in 2015 with a combination of cervical plexus block and interscalene brachial plexus block for clavicular surgery targeting the upper trunk. Twelve patients were enrolled in this study. The block was performed under ultrasound guidance with a single needle puncture using at least 10 ml of local anesthetic for the superficial cervical plexus block and 5–10 ml of local anesthetic for the interscalene brachial plexus block. This technique was described as “a new approach.” All the procedures were successfully completed under regional anesthesia alone without complications [8].

Shanthanna [9] reported two patients who successfully underwent clavicle surgery under general anesthesia combined with regional anesthesia. One of the patients was a 50-year-old woman with a history of pulmonary emphysema who had sustained a fall resulting in a fracture of her left clavicle. The other was a 37-year-old man with Steven-Johnson syndrome and a history of daily marijuana usage who underwent clavicle surgery due to severe pain arising from prior injuries and operative procedures. A superficial cervical plexus block and a selective C5 nerve root block was performed prior to general anesthesia to avoid possible complications related to the interscalene brachial plexus block and to minimize postoperative pain.

Open clavicle surgery with internal fixation needs careful anesthetic management. The sitting position and the difficult airway access during surgery pose challenges to the anesthesiologist. Anesthesiologists prefer regional anesthesia with ultrasound-guided superficial cervical plexus block combined with an interscalene brachial plexus block to avoid the complications associated with general anesthesia. Horner’s syndrome and phrenic nerve palsy are complications related to interscalene brachial plexus block that persuade anesthesiologists to perform selective nerve blocks using new approaches.

We performed a superficial cervical plexus block combined with supraclavicular brachial plexus block in our patient. Open clavicle surgery was performed successfully using this approach. No complications such as phrenic nerve palsy, Horner’s syndrome, or pneumothorax were encountered; besides, the patient experienced no pain. This approach may be successful in avoiding possible complications related to interscalene brachial plexus block. Future studies are required to establish the safety and efficacy of this technique.

**Conflicts of Interest**

No potential conflict of interest relevant to this article was reported.
Author Contributions

Onur Baran, MD (Writing – original draft)
Bünyamin Kir, MD (Writing – review & editing)
İrem Ateş, MD (Methodology)
Ayhan Şahin, Asst. Prof. (Methodology)
Ali Üzürk, MD (Resources)

ORCID

Onur Baran, https://orcid.org/0000-0003-0007-6315
Bünyamin Kir, https://orcid.org/0000-0001-6158-4351
İrem Ateş, https://orcid.org/0000-0001-9867-5011
Ayhan Şahin, https://orcid.org/0000-0002-3539-2353
Ali Üzürk, https://orcid.org/0000-0002-9947-5828

References

Sudden hemodynamic collapse after prone positioning on a Jackson spinal table for spinal surgery

Jae Hong Park, Ji Yeon Kwon, Sang Eun Lee, Yong Han Kim, Se Hun Kim

Department of Anesthesiology and Pain Medicine, Haeundae Paik Hospital, Inje University College of Medicine, Busan, Korea

Background: The prone position is used for a variety of procedures and surgeries, and hypotension is a commonly encountered complication.

Case: A 75-year-old obese woman with lumbar spinal stenosis underwent posterior lumbar spinal fusion and posterolateral interbody fusion under general anesthesia. Before the surgery, when she was positioned on a Jackson spinal table in the prone position, sudden severe hypotension and hemodynamic collapse developed. The circulatory collapse was refractory to intravascular volume expansion and administration of inotropes and vasopressors. However, the application of external abdominal support immediately restored hemodynamic stability. The patient successfully underwent the surgery using an external abdominal support, and no post-operative complication was noted, including abdominal compartment syndrome.

Conclusions: The Jackson spinal table allowed the abdomen to hang freely, providing abdominal decompression while resulting in a severely sagged abdomen. We suspected that the sagging abdomen had pulled the abdominal contents downwards, kinking the inferior vena cava or causing a venous pool in the abdomen, resulting in the obstruction of venous return to the heart.

Keywords: Circulatory collapse; General anesthesia; Obesity; Prone; Spinal stenosis; Systolic hypotension.

The prone position provides an excellent environment for surgical approach to the spine and dorsal anatomy. This position, however, can cause hemodynamic changes, such as decrease in arterial blood pressure, mainly due to decreases in stroke volume, cardiac index, and venous return [1-5]. This position also increases intra-abdominal pressure causing complications, such as abdominal compartment syndrome [4]. The Jackson spinal table (Mizuo ISO, USA) has minimal effects on cardiac function and decompresses the abdomen by allowing it to hang freely [4,5].

However, blood may pool in the splanchnic vessels of the abdomen when the it is allowed to hang freely, thereby decreasing venous return and leading to a reduction in cardiac output and systemic hypotension. This case report describes an obese patient who experienced sudden hypotension and hemodynamic collapse soon after prone positioning on a Jackson spinal table; the patient immediately recovered after the use of an external abdominal support.

Case Report

A 75-year-old female patient (weight 78 kg, height 152 cm, body mass index 33.7 kg/m²) with lumbar spinal stenosis in L1/2 and L2/3 was scheduled for an elective surgery.
involving posterior lumbar spinal fusion and posterolateral interbody fusion. Her previous medical history included diabetes mellitus and Parkinson’s disease. She had been on insulin and levodopa. She had no abnormalities in pre-operative evaluations.

General anesthesia was induced using intravenous propofol, remifentanil and rocuronium. After an uneventful endotracheal intubation, a left radial arterial catheter and a right internal jugular venous catheter were placed. Anesthesia was maintained using desflurane 6 vol% and remifentanil infusion at 0.1 μg/kg/min. The vital signs were as follows: arterial blood pressure, 107/69 mmHg; heart rate, 100 beats/min; respiration rate, 12 breaths/min; and peripheral capillary oxygen saturation (SpO\textsubscript{2}), 100%.

Before the surgery, the patient was positioned in the prone position on a Jackson spinal table. Her abdomen was allowed to hang freely, and severe sagging of the abdomen was observed (Fig. 1). Upon positioning, her arterial blood pressure suddenly dropped to 45/35 mmHg, and the arterial waveform soon disappeared. Heart rate increased by less than 10%, while a normal sinus rhythm was maintained on the electrocardiogram, and SpO\textsubscript{2} was 100%. End-tidal carbon dioxide, airway pressure, and body temperature remained unchanged.

The hemodynamic collapse was refractory to preload challenge using boluses of crystalloids. There was also no hemodynamic response to repetitive, dose-increasing boluses of ephedrine, phenylephrine, and even epinephrine. We suspected that these changes were due to mechanical causes that which might have disturbed her normal blood circulation and decided to lift her hanging sagged abdomen. When an external abdominal support was placed (Fig. 2), the arterial waveform and vital signs were rapidly restored.

Once hemodynamic stability was achieved, the surgery began and lasted for 6 hours uneventfully. Before changing her to the supine position, we reproduced the problematic situation by removing the external abdominal support; the abdomen hung freely again, and the sudden drop in arterial blood pressure and the disappearance of arterial wave reappeared. These events quickly disappeared when the external abdominal support was applied. The patient was returned to the supine position and extubated without any complications, including an increase in intra-abdominal pressure and development of abdominal compartment syndrome. She was admitted in the surgical intensive care unit for a day, and there was no other complication until discharge. The written informed consent for the use of images and details of the case for publication of this report has been obtained.

**Discussion**

Hypotension is a common complication observed during anesthesia and surgery. Common risk factors of intra-operative hypotension are deep anesthesia, hypovolemia, hemorrhage, heart failure and pulmonary embolism.

The prone position is used for a variety of procedures and surgeries, and hypotension is a commonly encountered complication. Several studies in the literature focused on physiologic changes, other than the above-mentioned risk factors, that result in hypotension when an individual is in the prone position. This position causes hypotension by decreasing stroke volume and cardiac index [1]. A decrease in preload is considered responsible for a reduction in stroke volume. Preload can be decreased by blood sequestration in dependent parts of the body, aortocaval compression, increased intrathoracic pressure with poor positioning and chest wall compression, and positive-pressure ventilation [2]. Significant pelvic and abdominal compressions cause an increase in intraabdominal pressure or direct compression of the inferior vena cava that leads to venous pooling and decreased venous return [3]. The increase in thoracic pressure reduces left ventricular compliance and filling, resulting in decreased ventricular volume, stroke volume, and cardiac index [4].

![Fig. 1. The patient’s abdomen in the prone position on a Jackson spinal table.](https://doi.org/10.4097/kja.d.18.00339)

![Fig. 2. The patient’s abdomen after applying an external abdominal support.](https://doi.org/10.4097/kja.d.18.00339)
Among several prone positioning systems, the Jackson spinal table produces minimal effects on cardiac function, including the cardiac index and stroke volume [5]. Moreover, the table allows the abdomen to hang freely that decreases the pressure on the abdomen, especially in obese patients. The external abdominal support is not usually recommended because it can cause changes in the compliance of the abdomen [6].

Sudden hemodynamic collapse is a rare complication in surgery in the prone position. Several cases of hemodynamic collapse manifesting sudden, profound, and refractory hypotension have been reported. Patients with anatomic deformities, such as pectus excavatum or Marfan’s-like features that could compress the thoracic cavity, developed intraoperative refractory hypotension [7-9]. In cases of scoliosis, mechanical compressions on the mediastinum and chest that led to loss of cardiac function and hemodynamic collapse, showing a feature of obstructive cardiogenic shock, were also reported [10,11]. These mechanical compressions were caused by anatomical deformities.

In this case, the patient had no anatomical deformities. Hypovolemia, decreased vascular resistance, and decreased cardiac contractility were ruled out by fluid challenge and the use of vaso-pressors and inotropes. Hypoxia did not occur and other vital signs and monitoring parameters including end-tidal carbon dioxide, airway pressure, and body temperature remained unchanged. All possible factors were ruled out, excluding the intraabdominal mechanical causes that inhibit venous return to the heart. Her severely sagged abdomen seemed to cause the sudden hemodynamic collapse. We suspected that this abdominal sagging pulled her abdominal wall and intraabdominal contents downwards, thus, leading to kinking of the inferior vena cava or blood sequestration in the abdomen. Subsequent sudden obstruction of inflow to the heart was then suspected to have caused the hemodynamic collapse. The hemodynamic instability was simply resolved by applying an external abdominal support, and it seemed to restore venous return.

Factors that increase intrathoracic or intraabdominal pressure cause hypotension and hemodynamic collapse. In obese patients, the distended abdomen can be compressed in the prone position, severely enough to increase intraabdominal pressure that can cause circulatory collapse with or without an abdominal compartment syndrome. The Jackson spinal table is widely used to prevent these complications. When the patient is placed on this table, less pressure is exerted on the abdomen, and the risk of increasing abdominal pressure and development of abdominal compartment syndrome is reduced.

However, in obese patients like the patient in this case, using the Jackson spinal table can cause kinking of a large vessel or severe blood sequestration in the abdomen by hanging the abdomen and pulling intraabdominal contents downwards. Although the application of an external abdominal support is not usually recommended in the prone position, this case showed that in some situations it may reduce the risk of hemodynamic instability. If hemodynamic collapse occurs with prone positioning, the application of an external abdominal support to lift up the hanging abdomen should be considered, and careful observation of the intraabdominal pressure is required.

**Conflicts of Interest**

No potential conflict of interest relevant to this article was reported.

**Author Contributions**

Jae Hong Park (Supervision; Writing-review and editing)  
Ji Yeon Kwon (Data curation; Validation)  
Sang Eun Lee (Conceptualization; Resource)  
Yong Han Kim (Conceptualization; Validation)  
Se Hun Kim (Writing-original draft)

**ORCID**

Jae Hong Park, https://orcid.org/0000-0003-0779-4483  
Ji Yeon Kwon, https://orcid.org/0000-0002-0170-577X  
Sang Eun Lee, https://orcid.org/0000-0002-9029-4991  
Yong Han Kim, https://orcid.org/0000-0001-6357-1036  
Se Hun Kim, https://orcid.org/0000-0002-2752-2883

**References**

Anesthetic management of a parturient with Behcet’s disease and suspected arrhythmogenic right ventricular dysplasia

Pietro Paolo Giuri, Gian Luigi Gonnella, Stefano Catarci, Mariano Ciancia, Gaetano Draisci

Department of Anesthesiology and Intensive Care Medicine, Catholic University School of Medicine, Rome, Italy

We present the anesthetic management of a 38-week parturient with Behcet’s disease (BD) complicated by a suspected arrhythmogenic right ventricular dysplasia (ARVD) undergoing labor epidural analgesia. A 31-year-old nulliparous patient with BD was hospitalized and labor induction was started. Twenty-four hours later after misoprostol administration, active labor began and the patient was admitted in the delivery room. On request, epidural analgesia was performed without complications. Although a spinal anesthesia for urgent cesarean section and epidural anesthesia for endovascular repair of abdominal aortic aneurysms have been already presented in the literature [1], this is the first report describing epidural analgesia for vaginal delivery in a patient with BD and suspected ARVD.

The patient was referred to the Anesthesia Preadmission Clinic at 35 weeks of gestation for suspected ARVD complicating BD. She weighed 67 kg and was 156 cm in height (body mass index: 27.57 kg/m²). At 4 years of age, she was diagnosed with BD characterized by oral and genital ulcers, folliculitis, erythema nodosum, and bowel inflammatory disease, and at 15 years of age, she was diagnosed with thrombosis in her arm. At 16 years of age, electrocardiogram (ECG) stress test for competitive sports showed T-negative waves from V1 to V4 and non-sustained ventricular tachycardia, and ARVD was suspected. A definitive ARVD diagnosis on cardiac magnetic resonance imaging (MRI) or endocardial biopsy has never been made. The patient’s ECG showed mild apical hypokinesia of the right ventricle and nonspecific hypoechoic pericardial image beside the right ventricular apex. The cardiology center where she was treated since her teen ages suggested an elective cesarean section despite the suspected diagnosis of ARVD. The patient presented with gastrointestinal symptoms, oral ulcers, and arthralgia for which she was started on steroids (prednisone 25 mg) in the 33rd week of gestation, which improved the symptoms. She had mild dyspnea without other cardiovascular symptoms since the previous two weeks. At 35th week of gestation, cardiologic and rheumatologic evaluations were planned. Rheumatologic consultation confirmed current steroid therapy and did not show any contraindication for vaginal delivery. After a 12-lead ECG showing sinus rhythm and T waves anomalies in the inferior leads, transthoracic echocardiogram showing normal systolic function (ejection fraction 66%), with limited lower septum akenisia and right ventricle middle-apical slight ectasia with tricuspid annular plane systolic excursion of 22 mm, and 24-hour Holter ECG showing infrequent ventricular and supraventricular ectopic beats, cardiological consultation concluded that in the absence of an obvious arrhythmic burden and without clear MRI signs of ARVD, there were no cardiological contraindications for vaginal delivery. The patient was discharged, and hospital-
ization at 38 weeks for labor induction was planned. After hospital readmission at 38 weeks, anesthesiologic assessment was performed. It focused on systems potentially affected by BD, such as the respiratory system, nervous system, and cardiovascular system, given the patient’s medical history. No difficulties were predicted in airway management, and no pathological findings were detected on neurological assessment. Cardiac involvement partially confirmed on previous cardiologic consultation did not show any contraindication to epidural analgesia. Preoperative blood results were within the normal ranges. The patient requested epidural analgesia, which was performed at the first attempt at the L3–4 level with an 18 G Tuohy needle. An epidural catheter was inserted, and 20 ml of 0.1% ropivacaine and 10 μg of sufentanil were administered. Adequate analgesia was achieved in 15 minutes. After 2 hours, with complete cervical dilatation, 15 ml of 0.15% ropivacaine was administered, and the delivery was carried out uneventfully after 30 minutes. The postpartum period was uneventful. During puerperium, 12-lead ECG, transthoracic echocardiogram, and Holter-ECG substantially confirmed prepartum results, except for rare ventricular ectopic beats, and beta-blockers was prescribed. The patient was discharged with the baby, 5 days after delivery, in good health. Three weeks later, she reported no neurological or cardiological complications or skin changes at the sites of intravenous cannula or epidural catheter placement.

BD is a chronic inflammatory disorder characterized by widespread vasculitis with recurrent oral and genital ulcers, ocular symptoms, and musculoskeletal, neurological, cardiac, pulmonary, and gastrointestinal system involvement. 'Neuro-Behcet' [2] is a difficult diagnosis, so neurological life-threatening involvement cannot be totally excluded. Cardiac involvement may occur as endocarditis, myocarditis, pericarditis, intracardiac thrombosis, endomyocardial fibrosis, and valvular diseases [3]. Endomyocardial involvement typically manifests as fibrosis on the right and/or left side of the heart [4]. Pregnancy has a positive effect on BD. Muco-cutaneous ulcerations are the most common flares [3].

A planned anesthesia management for a BD patient with endomyocardial involvement is challenging and with focus on airway, hemodynamics, and possible neuraxial manifestations can provide a favorable outcome. Airway management could be difficult owing to the oropharyngeal soft tissue ulcerations. Neuraxial techniques should be considered in patients without clinical signs or history of central nervous system involvement. Once BD has been diagnosed, accurate cardiovascular evaluation should be performed to exclude pericarditis, endocarditis, intracardiac thrombosis, myocardial infarction, endomyocardial fibrosis, and myocardial aneurysm.

In conclusion, epidural analgesia was safe and effective for our patient with BD, but anesthetic management should be performed based on the case, considering all implications of BD.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Pietro Paolo Giuri (Conceptualization, Writing–original draft) Gian Luigi Gonnella (Conceptualization, Supervision, Writing–review & editing) Stefano Catarci (Supervision, Writing–review & editing) Mariano Ciancia (Supervision, Writing–review & editing) Gaetano Draisci (Supervision, Writing–review & editing)

ORCID

Pietro Paolo Giuri, https://orcid.org/0000-0003-3644-1425 Gian Luigi Gonnella, https://orcid.org/0000-0002-7115-4408 Stefano Catarci, https://orcid.org/0000-0002-3466-6527 Mariano Ciancia, https://orcid.org/0000-0003-0474-2100 Gaetano Draisci, https://orcid.org/0000-0003-0148-5073

References

Sir, Fracture and migration of central venous catheter is a potentially dreadful complication, which requires early recognition and prompt intervention. Point-of-care ultrasonography (POCUS) is becoming an important tool for early localization and subsequent removal of foreign bodies in the body cavities [1,2]. This technique averts the need for X-ray or computed tomography (CT) imaging, and therefore, the associated radiation exposure. Embolization of fractured venous catheter in the external jugular vein (EJV) has been reported during patient movement, although a valve present at the end of the EJV halts this [3]. Migration of the fragment during the lag period between identification and retrieval causes great difficulty in its removal. POCUS enables real-time detection and correct localization immediately before surgical retrieval.

An 84-year-old male patient (written informed consent has been taken from the patient for publication) with diagnosis of pneumonia in the post-chemotherapy phase for acute myeloid leukemia was shifted to the intensive care unit for intermittent non-invasive ventilation. He had a 16-gauge external jugular venous catheter in situ, in view of difficult peripheral venous access. During removal, the catheter broke with the entire sheath inside the vein. Bedside POCUS in the intensive care unit was used to locate the catheter sheath (Fig. 1A). Surgical removal of the broken piece of the catheter was planned. Position of the fragment was re-confirmed by POCUS in the operation theatre just before retrieval, and was removed successfully under local anesthesia and monitored anesthesia care (Fig. 1B). Post-retrieval ultrasound was done to ensure the absence of remnants.

Various scenarios have been reported in relation to fractured intravenous catheters. Doley et al. [4] reported retrieval of a migrated fragment of an implanted central venous catheter through the neck surgically under fluoroscopic monitoring, after its initial detection by X-ray imaging.

A previous study reported fracture of central venous catheter and embolization into heart chambers and subsequently pulmonary vessels due to delayed detection and failure in early retrieval. [5]. Fluoroscopy with X-ray is considered the gold standard in retrieval of fractured catheters [4]. Nonetheless, we found that POCUS could be a suitable alternative for accurate detection and retrieval of broken catheter fragments. Therefore, we present the following advantages of POCUS:

1. Prompt localization of catheter position in case of suspected dislodgement, thus avoiding further displacement.
2. Avoids the need for radiological imaging like CT and shifting of the patient to the CT room, which may be difficult in critically ill patients.
3. Real-time imaging during removal helps to confirm position of the object, and ensures...
4. Confirms complete removal of the object after the procedure
5. Enables locating thrombus (if any), thereby guiding in taking necessary precautions.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Chitta Ranjan Mohanty (Conceptualization; Visualization; Writing – original draft; Writing – review & editing)
Suma Rabab Ahmed (Conceptualization; Writing – review & editing)
Anirudh Elyat (Writing – review & editing)
Snigdha Bellapukonda (Supervision; Writing – review & editing)
Sourav Kumar Panigrahi (Writing – review & editing)

ORCID

Chitta Ranjan Mohanty, https://orcid.org/0000-0002-8525-2084
Suma Rabab Ahmed, https://orcid.org/0000-0002-0750-2914
Anirudh Elyat, https://orcid.org/0000-0002-4090-5504
Snigdha Bellapukonda, https://orcid.org/0000-0003-1255-3238
Sourav Kumar Panigrahi, https://orcid.org/0000-0003-1083-0457

References

Complications during hysteroscopy for gynecological procedures: prevention is better than cure!

Nishkarsh Gupta¹, Anju Gupta²

¹Department of Onco-Anesthesiology and Palliative Medicine, Dr. B.R.A Institute-Rotary Cancer Hospital, All India Institute of Medical Sciences, ²Department of Anesthesiology and Critical Care, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

Hysteroscopy is the preferred method of diagnostic and therapeutic intervention for intrauterine pathologies. However, it may be associated with rare but serious complications such as venous air embolism (VAE), female transurethral resection of prostrate syndrome, fluid overload, uterine perforation, and hemorrhage.

We read with great interest the article, “Complications of fluid overload during hysteroscopic surgery,” by Hoffman et al. [1]. We commend the authors for the prompt diagnosis and successful management of a relatively rare complication. However, we have few concerns and suggestions in this regard.

Early signs of fluid overload in this case would be indicated by any measurable deficit in the input/output of the fluid used for distension and increase in venous pressures [2]. Mild pulmonary edema is reported with infusion of 800 ml of fluid under high pressure [3]. Two liters of isotonic normal saline used as the distention media in this case can surely lead to volume overload. However, the authors did not report the uterine distension pressure and difference in the volumes of the returning and purged fluids, which is important in cases of fluid overload and VAE [1].

The authors used laryngeal mask airway (LMA) for the prolonged surgery in the lithotomy and Trendelenburg positions, considering the possibility of fluid overload. However, the position recommended in these cases is supine/reverse Trendelenburg, and endotracheal intubation with positive-pressure ventilation should be performed [4,5]. In addition, the airway seal pressure at the time of insertion and during the event are not mentioned. The possibility of LMA displacement or laryngeal edema that can lead to inadequate ventilation cannot be ruled out.

The Trendelenburg position causes negative pressure in the pelvic veins and increases the risk of VAE, especially in spontaneously breathing patients. Positive pressure ventilation was not mentioned in the report prior to the event; thus, we can assume that both the conditions were prevailing, thereby increasing the risk of VAE in this patient.

Desaturation and hemodynamic instability occurred in the present case 150 minutes after induction, and the possibility of a VAE cannot be ruled out. Hysteroscopy-related VAE is a relatively common occurrence, with a high reported incidence of 10–50% [5]. However, most of such VAE events are clinically insignificant, as the liver might be acting as a filter reducing the amount of air reaching the pulmonary circulation. The characteristic clinical features include decreased end-tidal carbon dioxide (EtCO₂) concentration, desaturation, bradycardia, tachycardia, “mill wheel” murmur, bronchosospasm, and respiratory and cardiac arrest [4,5]. Other characteristic clinical features include increased pulmonary arterial and central venous pressures, decreased blood pressure, electrocardiogram (ECG) changes, decreased arterial partial pressure of oxygen, and a widened gap.
between the arterial pressure of carbon dioxide (PaCO$_2$) and EtCO$_2$. Use of continuous EtCO$_2$ has been recommended for hysteroscopy cases [4,5]. The authors have documented only desaturation, hemodynamic instability, hypercapnia (PaCO$_2$ of 49 mmHg) with no reference to EtCO$_2$ values, ECG changes, murmur, hypotension, or bradycardia at the time of the event [1]. The patient had bronchospasm, which can occur consequent to VAE and lead to increased peak airway pressures as noted in this case. On these grounds, we would put forward the argument that the present scenario could well be a non-fatal sequel of VAE rather than fluid overload.

The other arguments in favor of air embolism in the present case include the sudden catastrophic occurrence of hemodynamic instability with desaturation, lithotomy in the Trendelenburg position, probable spontaneous respiration during the event (positive pressure initiated after the event), and large uterine fibroids with the possibility of opening up the uterine sinuses. The patient had large uterine fibroids, and any uterine injury exposing large venous sinuses is the usual inciting factor of VAE [1]. Surgeons should maintain a close communication with anesthetists and inform the occurrence of even minor injuries. In this report, surgical complications were not ruled out. An echocardiography should have been performed after the event, which could reveal dilatation of the right side of the heart and elevated pulmonary artery pressure along with preserved left ventricular function in case of VAE.

Certain precautions have been suggested to reduce the incidence of VAE in hysteroscopy, such as the use of a mechanical pump with Y connectors, pressure monitoring system (keep < 100 mmHg), use of advanced hemodynamic monitoring, restricting the height of the fluid bottles to < 1 m, keeping the hysteroscope set free of air, airtight connections, early termination of the procedure if the infusion fluid deficit is > 1,000 ml with sorbitol or > 1,500 ml with saline, and avoiding the use of external pressure infusers [2,4,5]. In addition, surgeons should keep the cervix occluded at all times after dilation and avoid repeated reinsertions of the hysteroscope.

In such cases, rapid identification and prevention of further gas entrainment into the circulation is crucial to the ultimate patient survival. The surgery should be stopped immediately, the uterus should be deflated, and a dilator or wet gauzes should be used to occlude the vagina. In addition, the patient should immediately be placed in the reverse Trendelenburg position to raise the level of the heart above the site of air entry, reducing further air entrainment.

Hence, we urge utmost caution and vigilance in managing these cases to reduce morbidity and mortality. Appropriate protocols and training should be in place to prevent such mishaps.

**Conflicts of Interest**

No potential conflict of interest relevant to this article was reported.

**Author Contributions**

Nishkarsh Gupta (Data curation; Writing–review & editing)
Anju Gupta (Data curation; Writing–review & editing)

**ORCID**

Anju Gupta, https://orcid.org/0000-0003-1726-1488
Nishkarsh Gupta, https://orcid.org/0000-0002-8444-2564

**References**

To the authors of 'Complications during hysteroscopy for gynecological procedures: prevention is better than cure!'

Christopher Hoffman

Department of Anesthesiology & Perioperative Medicine, Drexel University College of Medicine, Hahnemann University Hospital, Philadelphia, PA, USA

To the authors of 'Complications during hysteroscopy for gynecological procedures: prevention is better than cure!'

Thank you for reading and responding to our article, 'Complications of fluid overload during hysteroscopic surgery [1].' We appreciate the interest in our work and invite questions and concerns relevant to this topic. To that effect, we would like to address points made in your response. We will address them in the order introduced.

We agree that 'prevention is better than cure.' We reported 1,300 ml of intravenous fluid administration. Hysteroscopic fluid medium of 2,010 ml was introduced, with 700 ml evacuated via Foley catheter. There may be unmeasured fluid lost via extravasation, which was not measured or documented. Nevertheless, we agree that this total fluid amount, though administered over two and a half hours, warrants concern. This concern was the focal point of our case report. We agree that communication of the volume administered in real-time is key to preventing subsequent complications. We express concern with the specifics discussed and citations referenced in your response. You cited primary source material in stating that pulmonary edema was reported with infusions of 800 ml of fluid under high pressure [2]. This article does not state this. The authors state that their results were either not analyzed statistically or that the average fluid deficits were clinically insignificant. No fluid recommendations were given. The background material cited does not address intravasation goals for isotonic fluids like the normal saline utilized in our case.

The authors of this letter state that it is recommended to establish endotracheal intubation and positive pressure ventilation during hysteroscopy, given the lithotomy and Trendelenburg positions.

The two articles cited for this proposed standard of care are low levels of evidence. The first is a summary of 13 cases with varying and/or absent documentation of surgical diagnosis, anesthetic modality, distension media, and patient positioning. We also note no formal recommendation of endotracheal intubation is given in this article [3]. The second article cited discloses three case reports describing venous air embolism (VAE) with subsequent recommendation to intubate all hysteroscopic cases [4]. Those authors disclose that all three cases occurred despite endotracheal intubation and that two of the three occurred after instituting intubation as a protocol for hysteroscopy. Endotracheal intubation institution in this article lacks statistical evidence of causality or correlation. A variety of recommendations have been made in prior publications. Local and/or neuraxial anesthesia to detect symptomatology in awake patients is a reported recommendation [5]. The aforementioned cited case summary includes patients receiving this modality. Those authors imply an escalation of airway intervention is necessary when acuity or co-
morbidity rises [3]. We would therefore respond by stating that a risk stratification to consider endotracheal tube placement should be made on a case by case basis.

The authors note that the airway seal pressure at the time of laryngeal mask airway (LMA) insertion and at the time of the event are not mentioned and the possibility of LMA displacement or laryngeal edema leading to inadequate ventilation cannot be ruled out. We can report that LMA placement and seal appeared unremarkable during the entirety of this case. We would agree that undetected placement or sealing complications with any airway device, LMA or endotracheal tube, is a potential complication that could occur in this setting.

The authors comment that the Trendelenburg position and spontaneous ventilation increased the risk of VAE. Responding authors cited hysteroscopy-related VAE to occur as high as 10–50% of cases [3]. The cited case summary references seven articles, most of which are case reports referring to VAE occurring during CO2 utilization for distension media. Background source material selection bias may be evident. For example, cursory background searching yields sources citing gas embolism occurring in 0.017% hysteroscopies with CO2, as the distending medium specifically. They state CO2 should be contraindicated during hysteroscopy for this purpose. They note that room air may be accidentally introduced in poorly controlled fluid intravasation systems, but they do not state that this could elevate the incidence of VAE from 0.017% to 10–50% [6]. Our posed respiratory complications secondary to fluid overload is a more common occurrence. The same paper that cited 0.017% gas embolism occurrence cites 0.14% fluid overload occurrence [6]. Even if gas distention media was utilized or accidentally introduced to our fluid intravasation equipment, we note that the source material cited reports that fluid overload is 8.2 times more likely to occur.

The authors present the symptoms associated with VAE. We would agree that hemodynamic changes, desaturation, and respiratory difficulty occurred in this case. The other clinical features included, namely ‘mill wheel’ murmur and electrocardiographic changes, did not. We did report hypercapnia and moderate hypoxemia (arterial blood gas yielded partial pressure of carbon dioxide 49.5 mmHg and partial pressure of oxygen 327 mmHg on 100% fraction of inspired oxygen). Crackles on chest auscultation and chest radiography exhibiting bilateral patchy opacification suggests pulmonary edema secondary to fluid overload. These findings are not uniformly evident with VAE. We also note the timeline of recovery. VAE significant enough to elicit hemodynamic compromise and ventilation/oxygenation limitation does not recover quickly. Specific time to recovery is not widely documented, but recommendations of VAE treatment (e.g., hyperbaric oxygen therapy) is commonly reported in iterations of hours to days. The patient discussed returned to baseline and was extubated 5 hours post procedure. The apparent absence of entrained air in the intravasation system, constellation of clinical features, and timeline of recovery do not support a diagnosis of VAE.

We agree that precautions discussed in your letter to prevent VAE are mandatory. We agree that rapid identification and prevention of further gas embolus is key to limiting catastrophic outcomes. In this case, we highlight the importance of maintaining vigilance with reference to inadvertently escalated fluid administration. Communication with the surgical team regarding the possible concerns for fluid overload and a meticulous attention to patient hemodynamic patterns via noninvasive or invasive monitors is warranted.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

References

We read the case report titled ‘Anaphylactic shock after sugammadex administration, induced by formation of a sugammadex-rocuronium complex by Kim et al. [1] with great interest. As a result of their effective treatment, the patient fortunately, recovered. To find the causative agent of anaphylactic shock, the authors performed skin tests four days after anaphylaxis. However, it is recommended that skin testing is conducted at least four to six weeks after the occurrence of a suspected perioperative allergic reaction [2]. This time interval allows for the resolution of clinical symptoms and clearance of the suspected drugs and anti-allergic medications [3]. Skin tests performed earlier than this can result in a negative reaction due to mediator depletion after anaphylaxis. When tests are performed earlier than four weeks, only positive skin test results are useful and a negative skin test needs to be interpreted with caution. Therefore, the authors’ skin test was done too early and there is doubt about its reliability.

Generally, appropriate positive and negative controls are always necessary in skin tests for suspected hypersensitivity reactions to confirm skin reactivity [4]. Usually, histamine is used as a positive control and saline as a negative control. Unfortunately, the authors did not include a positive control in their test. If the patient had shown a negative response to histamine, the patient’s negative response to sugammadex should be a false result.

Certain drugs also decrease skin test responses and must be discontinued prior to a skin test. Antihistamines and glucocorticoids fall into this category. Five days of drug-free intervals after H1-antihistamines and three days after less than 50 mg of short-term prednisolone are recommended because those drugs can decrease skin test reactivity [4]. Whether short and long-term systemic corticosteroids need to be stopped prior to testing is controversial [5]. The authors administered 60 μg/kg of dexamethasone and 50 μg/kg of chlorpheniramine after anaphylaxis. In addition to the skin test performed too early, drugs decreasing skin reactivity might have contributed to the negative response to all drugs.

If testing is performed earlier than four to six weeks, repeat testing after four to six weeks may be considered. In the case of negative skin test results, a second evaluation is advisable. The authors performed a skin test to sugammadex-rocuronium complex after a month. If the authors performed a skin test for sugammadex again with the sugammadex-rocuronium complex, the results would have been very clear. In our opinion, the interpretation of skin tests in this report was not complete because the skin tests did not meet the conditions of adequate timing after anaphylaxis and the appropriate use of positive and negative controls.

Presently, there are no established guidelines for skin testing for anaphylaxis to sugammadex. The reported allergenic epitopes were sugammadex, gamma-cyclodextrin, or sugammadex-rocuronium complex. Accurate skin tests using positive and negative controls at the right time will be helpful to identify the allergenic epitopes of sugammadex.
Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Sung Jin Hong (Conceptualization; Investigation; Supervision)
Ji Yung Lee (Writing – original draft, review & editing)

ORCID

Sung Jin Hong, https://orcid.org/0000-0001-9353-2644
Ji Yung Lee, https://orcid.org/0000-0001-9123-1135

References

Effects of sevoflurane on neuronal cell damage after severe cerebral ischemia in rats

Hee-Pyoung Park, Eun-Ju Jeong, Mi-Hyun Kim, Jung-Won Hwang, Young-Jin Lim, Seong-Won Min, Chong-Soo Kim, Young-Tae Jeon

The article by Park HP, et al. entitled, “Effects of sevoflurane on neuronal cell damage after severe cerebral ischemia in rats.” (Korean J Anesthesiol 2011 October; 61(4): 327-31) was published incorrectly in third author's Name and Institution.

Mi-Hyun Kim
Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, Seoul, Korea.

This should be corrected as follows;

Mihyun Kim
Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital, Seongnam, Korea.
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For the policies on research and publication ethics that are not stated in these instructions, the Good Publication Practice Guidelines for Medical Journals, available at: www.kamje.or.kr/intro. php?body=publishing_ethics, or the Guidelines on Good Publication, available at: publicationethics.org/, can be applied.

1. **Conflict-of-interest statement**
Conflict of interest exists when an author or the author’s institution, reviewer, or editor has financial or personal relationships that inappropriately influence or bias his or her actions. Such relationships are also known as dual commitments, competing interests, or competing loyalties. These relationships vary from being negligible to having a great potential for influencing judgment. Not all relationships represent true conflict of interest. On the other hand, the potential for conflict of interest can exist regardless of whether an individual believes that the relationship affects his or her scientific judgment. Financial relationships such as employment, consultancies, stock ownership, honoraria, and paid expert testimony are the most easily identifiable conflicts of interest and the most likely to undermine the credibility of the journal, the authors, or of the science itself. Conflicts can occur for other reasons as well, such as personal relationships, academic competition, and intellectual passion (http://www.icmje.org/conflicts-of-interest/). If there are any conflicts of interest, authors should disclose them in the manuscript. The conflicts of interest may occur during the research process as well; however, it is important to provide disclosure. If there is a disclosure, editors, reviewers, and reader can approach the manuscript after understanding the situation and the background of the completed research.

2. **Statement of informed consent and Institutional Review Board approval**
If the study in the article is on human subjects or human-originated material, informed consent for the study and the IRB approval number needs to be provided. Copies of written informed consents and Institutional Review Board (IRB) approval for clinical research should be kept. If necessary, the editor or reviewers may request copies of these documents to make potential ethical issues clear.

3. **Statement of human and animal right**
Clinical research should be done in accordance of the Ethical Principles for Medical Research Involving Human Subjects, outlined in the Helsinki Declaration of 1975 (revised 2018) (available from: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/). Clinical studies that do not meet the Helsinki Declaration will not be considered for publication. Human subjects should not be identifiable, such that patients’
names, initials, hospital numbers, dates of birth, or other protected healthcare information should not be disclosed. For animal subjects, research should be performed based on the National or Institutional Guide for the Care and Use of Laboratory Animals, and the ethical treatment of all experimental animals should be maintained.

4. Registration of the clinical trial research
Any researches that deals with clinical trial should be registered with the primary national clinical trial registration site such as Korea Clinical Research Information Service (cris.nih.go.kr/) or other sites accredited by WHO or International Committee of Medical Journal Editor such as ClinicalTrials.gov (clinicaltrials.gov/).

5. Reporting guidelines
The KJA recommends a submitted manuscript to follow reporting guidelines appropriate for various study types. Good sources for reporting guidelines are the Enhancing the QUAlity and Transparency Of health Research (EQUATOR) Network (www.equator-network.org/) and the U.S. National Library of Medicine's (NLM's) Research Reporting Guidelines and Initiatives (www.nlm.nih.gov/services/research_report_guide.html).

6. Authorship
Authorship credit should be based on: 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; AND 2) drafting the article or revising it critically for important intellectual content; AND 3) final approval of the version to be published; AND 4) agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Authors should meet these 4 conditions. If the number of authors is equal to or greater than 2, there should be a list of each author's role in the submitted paper. Authors are obliged to participate in peer review process. All others who contributed to the work who are not authors should be named in the Acknowledgements section. KJA has a strict policy on changes to authorship after acceptance of the article and will only consider changes in the most extraordinary situations once the article is accepted.

7. Plagiarism and duplicate publication
Plagiarism is the use of previously published material without attribution. The KJA editorial office screens all submitted manuscripts for plagiarism, using a sophisticated software program, prior to peer review. When plagiarism is detected at any time before publication, the KJA editorial office will take appropriate action as directed by the standards set forth by the Committee on Publication Ethics (COPE). For additional information, please visit http://www.publicationethics.org. It is mandatory for all authors to resolve any copyright issues when citing a figure or table from a different journal that is not open access.

8. Secondary publication
It is possible to republish manuscripts if the manuscripts satisfy the condition of secondary publication of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, available at: www.icmje.org/.

9. Feedback after publication
If the authors or readers find any errors, or contents that should be revised, it can be requested from the Editorial Board. The Editorial Board may consider erratum, corrigendum or a retraction. If there are any revisions to the article, there will be a CrossMark description to announce the final draft. If there is a retraction, a reader's opinion on the published article with the form of Letter to the editor, it will be forwarded to the authors. The authors can reply to the reader's letter. Letter to the editor and the author's reply may be also published.

9-1. Process to manage the research and publication misconduct
When the Journal faces suspected cases of research and publication misconduct such as a redundant (duplicate) publication, plagiarism, fabricated data, changes in authorship, undisclosed conflicts of interest, an ethical problem discovered with the submitted manuscript, a reviewer who has appropriated an author's idea or data, complaints against editors, and other issues, the resolving process will follow the flowchart provided by the Committee on Publication Ethics (http://publicationethics.org/resources/flowcharts). The Editorial Board of KJA will discuss the suspected cases and reach a decision. KJA will not hesitate to publish errata, corrigenda, clarifications, retractions, and apologies when needed.

9-2. Policy of Article withdrawal, retraction, and replacement
1) Article withdrawal
Articles in Press (articles that have been accepted for publication but which have not been formally published and will not yet have the complete volume/issue/page information) that include errors, or are discovered to be accidental duplicates of other published article(s), or are determined to violate our journal publishing ethics guidelines in the view of the editors (such as multiple submission, bogus claims of authorship, plagiarism,
fraudulent use of data or the like), may be “Withdrawn”.

2) Article retraction
Errors serious enough to invalidate a paper’s results and conclusions (Infringements of professional ethical codes, such as multiple submission, bogus claims of authorship, plagiarism, fraudulent use of data or the like) may require retraction.

3) Article replacement
Replacement (retraction with republication) can be considered in cases where honest error (e.g., a misclassification or miscalculation) leads to a major change in the direction or significance of the results, interpretations, and conclusions. If the error is judged to be unintentional, the underlying science appears valid, and the changed version of the paper survives further review and editorial scrutiny, then replacement of the changed paper, with an explanation, allows full correction of the scientific literature.

See also the National Library of Medicine’s policy on retractions and the recommendations of the International Committee of Medical Journal Editors (ICMJE) concerning corrections and retractions, or https://publicationethics.org/resources/guidelines.

9-3. Appeals and complaints
KJA adheres to COPE guidelines regarding appeals to editorial decisions and complaints. For additional information, please visit https://publicationethics.org/core-practices.

Data sharing statement

Manuscript preparation
1. Word processors and format of manuscript
A manuscript must be written in proper and clear English. The manuscript, including tables and their footnotes, and figure legends, must be typed in one double space. Materials should be prepared with a standard 12-point typeface or greater (Times New Roman typeface is preferred). The manuscript should be in the following sequence: cover letter (optional), title page file, manuscript (title and running title, abstract and keywords, introduction, materials and methods, results, discussion, references, tables, and figure legends), figures, other submission elements. All pages should be numbered consecutively starting from the title page. All numbers should be written in Arabic numerals throughout the manuscripts. Our preferred file format is DOCX or DOC. A single PDF file containing all materials in a file including figures and figure legends. In that case, authors should add line numbers throughout the document. Manuscript containing anything in headers and footers, except of page numbers, will be returned to authors. If your PDF submission is accepted, you will be asked to upload your final document file in DOCX or DOC format as well. Make sure to update your PDF file with the most recent version of your manuscript.

2. Abbreviation of terminology
Abbreviations should be avoided as much as possible. When they are used, full expression of the abbreviations following the abbreviated word in parentheses should be given at the first use. Common abbreviations, however, may be used, such as DNA. Abbreviation can be used if it is listed as a MeSH subject heading (http://www.ncbi.nlm.nih.gov/mesh).

3. Word-spacing
1) Leave 1 space for each side, using arithmetic marks as +, −, ×, etc.
   Leave no space for hyphen between words.
2) Leave 1 space after “,” and “;”. Leave 2 spaces after “.” and “:”.
3) Using parentheses, leave 1 space each side.
4) Brackets in parentheses, apply square brackets.

4. Citations
1) If a citation has 2 authors, write as “Hirota and Lambert.” If there are more than 3 authors, apply ‘et al.’ at the end of the first author’s surname. Ex) Kim et al. [1].
2) Citation should be applied after the last word or author’s surname.
3) Apply citation before a comma or period.
4) Identify reference by several or coupled Arabic numbers, enclosed in square brackets on the line as [1,3,5].

5. Arrangement of manuscript
ALL articles should be arranged in the following order.
6. Statistical Analysis

1) Describe the statistical tests employed in the study with enough detail so that readers can reproduce the same results if the original data are available. The name and version of the statistical package should be provided.

2) Authors should describe the objective of the study and hypothesis appropriately. The primary/secondary endpoints are predetermined sensibly according to the objective of the study.²

3) The characteristics of measured variables should determine the use of a parametric or nonparametric statistical method. When a parametric method is used, the authors should describe whether the basic statistical assumptions are met.² ³

4) For an analysis of a continuous variable, the normality of data should be examined. Describe the name and result of the particular method to test normality.

5) When analyzing a categorical variable, if the number of events and sample is small, exact test or asymptotic method with appropriate adjustments should be used. The standard chi-squared test or difference-in-proportions test may be performed only when the sample size and number of events are sufficiently large.

6) The Korean Journal of Anesthesiology (KJA) strongly encourages authors to show confidence intervals. It is not recommended to present the P value without showing the confidence interval. In addition, the uncertainty of estimated values, such as the confidence interval, should be described consistently in figures and tables.²

7) Except for study designs that require a one-tailed test, for example, non-inferiority trials, the P values should be two-tailed. A P value should be expressed up to three decimal places (not as “P < 0.05”). If the value is less than 0.001, it should be described as “P < 0.001” but never as “P = 0.000.” For large P value greater than 0.1, the values can be rounded off to one decimal place, for example, P = 0.1, P = 0.9.

8) A priori sample size calculation should be described in detail.² Sample size calculation must aim at preventing false negative results pertaining to the primary, instead of secondary, endpoint. Usually, the mean difference and standard deviation (SD) are typical parameters in estimating the effect size. The power must be equal to or greater than 80 percent. In the case of multiple comparisons, an adjusted level of significance is acceptable.²

9) When reporting a randomized clinical study, a CONSORT-type flow diagram, as well as all the items in the CONSORT checklist, should be included. If limited in terms of the space of the manuscript, this information should be submitted as a separate file along with the manuscript.²

10) Results must be written in significant figures. The measured and derived numbers should be rounded off to reflect the original degree of precision. Calculated or estimated numbers (such as mean and SD) should be expressed in no more than one significant digit beyond the measured accuracy. Therefore, the mean ± SD of body weight in patients measured on a scale that is accurate to 0.1 kg should be expressed as 65.45 ± 2.52 kg.

11) Except when otherwise stated herein, authors should conform to the most recent edition of the American Medical Association Manual of Style.⁴

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⁶Lee S and Lee DK. What is the proper way to apply the multiple comparison test? Korean J Anesthesiol 2018; 71: 353-60.
7. Organization of manuscript

1) Clinical or experimental research

(1) Title page

① Title
Title should be concise and precise.
For the title, only the first letter of the first word should be capitalized.

② Author information
First name, middle initial, and last name of each author, with their highest academic degree(s) (M.D., Ph.D., etc.), and institutional affiliations; make sure the names of and the order of authors as they appear on the Title Page and entered in the system match exactly.

③ Running title
A running title of no more than 40 characters, including letters and spaces, should be described. If inappropriate, the editorial board may revise it.

④ Corresponding Author
Name, mailing address, phone number, and e-mail address of the corresponding author

⑤ Previous presentation in conferences
Title of the conference, date of presentation, and the location of the conference may be described.

⑥ Conflict of interest
It should be disclosed here according to the statement in the Research and publication ethics regardless of existence of conflict of interest. If the authors have nothing to disclose, please state: “No potential conflict of interest relevant to this article was reported.”

⑦ Funding
Funding to the research should be provided here. Providing a FundRef ID is recommended including the name of the funding agency, country and if available, the number of the grant provided by the funding agency. If the funding agency does not have a FundRef ID, please ask that agency to contact the FundRef registry (e-mail: fundref.registry@crossref.org). Additional detailed policy of FundRef description is available from http://www.crossref.org/fundref/.

⑧ Acknowledgments
Any persons that contributed to the study or the manuscript, but not meeting the requirements of an authorship could be placed here. For mentioning any persons or any organizations in this section, there should be a written permission from them.

⑨ IRB number

⑩ Clinical trial registration number

If any of these elements are not applicable to your submission, write “not applicable” after the number and topic; for example, “Prior Presentations: Not applicable.”

(2) Manuscript

① Title and Running title

② Abstract
All manuscripts should contain a structured abstract that is written only in English. Provide an abstract of no more than 250 words. It should contain 4 subsections: Background, Methods, Results, and Conclusions. Quotation of references is not available in the abstract. A list of keywords, with a minimum of 6 and maximum of 10 items, should be included at the end of the abstract. The selection of keywords should be from MeSH (http://www.ncbi.nlm.nih.gov/mesh) and should be written in small alphabetic letters with the first letter in capital letter. Separate each word by a semicolon (;), and mark a period (.) at the end of the last word.

③ Introduction
The introduction should address the purpose of the article concisely and include background reports that are relevant to the purpose of the paper.

④ Materials and methods

· The materials and methods section should include sufficient details of the design, subjects, and methods of the article in order, as well as the data analysis methods and control of bias in the study. Sufficient details need to be addressed in the methodology section of an experimental study so that it can be further replicated by others.

· When reporting experiments with human or animal subjects, the authors should indicate whether they received approval from the Institutional Review Board for the study and the IRB approval number needs to be provided. When reporting experiments with animal subjects, the authors should indicate whether the handling of the animals was supervised by Institutional Board for the Care and Use of Laboratory Animals. “American Society of Anesthesiologists physical status classification” should not be abbreviated. As a rule, subsection titles are not recommended.

· Clearly describe the selection of observational or experimental participants. Ensure correct use of the terms sex (when reporting biological factors) and gender (identity, psychosocial or cultural factors), and, unless inappropriate,
report the sex and/or gender of study participants, the sex of animals or cells, and describe the methods used to determine sex and gender. If the study was done involving an exclusive population, for example in only one sex, authors should justify why, except in obvious cases (e.g., prostate cancer). For additional information, please visit http://www.icmje.org/about-icmje/faqs/icmje-recommendations/.

- Units

Laboratory information should be reported in International System of Units [SI]. Please refer to A Guide for Biological and Medical Editors and Authors, 6th Edn. Baron DN and Clarke HM, ed. (2008), CRC Press. or visit http://www.icmje.org/about-icmje/faqs/icmje-recommendations/

- Exceptions

A. The unit for volume is “L”, others in “dl, ml, μl”.
B. The units for pressure are mmHg or cmH2O.
C. Use Celsius for temperature
D. Units for concentration are M, mM, μM.
E. When more than 2 items are presented, diagonal slashes are acceptable for simple units. Negative exponents should not be used.
F. Leave 1 space between number and units.

Exception) 5%, 36°C

- Drug Names and Equipment

Use generic names. If a brand name must be used, insert it in parentheses after the generic name. Provide ® or ™ as a superscript and manufacturer’s name, and country.

- Ions

Ex) Na⁺ [O], Mg²⁺ [O], Mg²⁺ [X], Mg⁺² [X]

- Statistics

Statistical methods must be described with enough detail so that readers can reproduce the same results if the original data available. The KJA strongly encourages authors to show confidence intervals. It is not recommended to present the P value without showing the confidence interval. A sample size calculation should be described in detail. Sample size calculation must aim at preventing false negative results pertaining to the primary, instead of secondary, endpoint.

- Results

Results should be presented in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Do not repeat all of the data in the tables or illustrations in the text; emphasize or summarize only the most important observations. Results can be sectioned by subsection titles but should not be numbered. Citation of tables and figures should be provided as Table 1 and Fig. 1.

- Discussion

The discussion should be described to emphasize the new and important aspects of the study, including the conclusions. Do not repeat the results in detail or other information that is given in the Introduction or the Results section. Describe the conclusions according to the purpose of the study but avoid unqualified statements that are not adequately supported by the data. Conclusions may be stated briefly in the last paragraph of the Discussion section.

- References


- References should be obviously related to documents and should not be exceed 50. For exceeding the number of references, it should be negotiated with the Editorial Board. References should be numbered consecutively in the order in which they are first mentioned in the text. Provide footnotes in the body text section. All of the references should be stated in English, including author, title, name of journal, etc.

- If necessary, the editorial board may request original documents of the references.


- Six authors can be listed. If more than 6 authors are listed, only list 6 names with ‘et al.’

- Provide the start and final page numbers of the cited reference.

- Abstracts of conferences are not allowed to be included in the references. The American Society of Anesthesiologists (ASA) refresher course lecture is not acceptable as a reference.

- Description format

A. Regular journal

Author name. Title of journal Name of journal published year; volume: start page–final page.

B. Monographs
∙ If reference page is only 1 page, mark ‘p’.
∙ Mark if it is beyond the 2nd edition.
C. Chapter
D. Electronic documents
E. Online journal article
F. Papers that have been submitted and accepted for publication should be included in the list, with the phrase ‘in press’ replacing volume and page number. Authors should be prepared to give the volume and page number at the time of proof correction.
© Table
∙ Type or print each table on a separate sheet of paper.
∙ Number tables consecutively in the order of their first citation in the text.
∙ Supply a brief title
Tables should be more than 4 rows and should not be over 1 page.
∙ Except for titles and first letters, all of the text in the tables should be written in small alphabetic letters.
∙ In demographic data, sex would be provided as M/F, and age in yr. Data of year, weight, height, and any other units would be provided with 1 decimal place.
∙ “±” sign in the upper column of table should be lined up with the lower column.
∙ Footnotes should be provided consecutively in order of the cited tables or statistics.
∙ Marks for footnote should be given in order of *, †, ‡, §, II, §, **, ††, ‡‡... When marks are used to explain items of the table, indicate them with superscripts.
∙ Define all abbreviations except those approved by the International System of Units. Define all abbreviations every time they are repeated.
© Legends for figures and photographs
∙ All of the figures and photographs should be described in the text separately.
∙ The description order is the same as in the footnotes in tables and should be in recognizable sentences.
∙ Define all abbreviations every time they are repeated.
③ Figures and illustrations
① The KJA publishes in full color, and encourages authors to use color to increase the clarity of figures. Please note that color figures are used without charge for online reading. However, since it will be charged upon the publication, authors may choose to use colors only for online reading.
② Standard colors should be used (black, red, green, blue, cyan, magenta, orange, and gray). Avoid colors that are difficult to see on the printed page (e.g., yellow) or are visually distracting (e.g., pink). Figure backgrounds and plot areas should be white, not gray. Axis lines and ticks should be black and thick enough to clearly frame the image. Axis labels should be large enough to be easily readable, and printed in black.
③ Figures should be uploaded as separate tif, jpg, pdf, gif, ppt files. Width of figure should be 84 mm (one column). Contrast of photos or graphs should be at least 600 dpi. Contrast of line drawings should be at least 1,200 dpi. Number figures as “Fig. (Arabic numeral)” in the order of their citation. (ex. Fig. 1).
Photographs should be submitted individually. If Figure 1 is divided into A, B, C and D, do not combine it into 1, but submit each of them separately. Authors should submit line drawings in black and white.

In horizontal and vertical legends, the letter of the first English word should be capitalized.

Connections between numbers should be denoted by “-”, not “~“. Do not space the numbers (ex. 2–4).

Figures (line drawings) should be clearly printed in black and white.

Figures should be explained briefly in the footnotes. The format is the same as the table format.

An individual should not be recognizable in the photographs or X-ray films unless written consent of the subject has been obtained and is provided at the time of submission.

Pathological samples should be pictured with a measuring stick.

(4) Other submission elements (Video submission)

The KJA publishes supplemental video (movie) clip(s) that will be available online. Not only recording of the abstract, text, audio or video files, but also data files should be added here.

Each video clip should clearly illustrate the primary findings within an adequate amount of viewing time and be discussed in the text. Authors should provide appropriate labeling (e.g., arrows, abbreviations of anatomic structures, etc.) in the video clips. However, all identifying information, including patient name and/or ID number, hospital name, and date of the procedure, should be removed.

Video clips should contain succinct teaching points that must be supported by the current literature or standard reference texts, preferably those most accessible to the general reader. The adequacy of the teaching points will be evaluated during the review process and finally confirmed by the editorial board at the end of the review process.

Video clips are uploaded as the last file(s) at the time of manuscript submission and should be marked as supplementary video files.

The video clip(s) should have simple file names (e.g., Video 1***, Video 2****) and include the appropriate extension (e.g., .mov, .mpg).

The maximum number of video clips is 20.

The video clip(s) should be playable on both Windows and MAC computers. The video clip(s) should be tested for playback before submission, preferably on computers not used for their creation, to check for any compatibility issues.

Individual video files should be a minimum of 480 x 320 pixels (smaller clips will not be accepted) and a maximum of 2 GB. Files of < 15 MB will be rejected outright unless special arrangements have been made with the editorial board prior to submission. Approval of files of > 2 GB will be made at the end of the review process.

Supplemental still images that correspond to the respective video clip(s) should be, but are not always required to be, accompanied by legends. The video clip file name(s) should refer to the corresponding figure number(s).

2) Case Reports

A case report is almost never a suitable means to describe the efficacy of a treatment or a drug; instead, an adequately powered and well-controlled clinical trial should be performed to demonstrate such efficacy. The only context in which a case report can be used to describe efficacy is in a clinical scenario, or population, that is so unusual that a clinical trial is not feasible.

Case reports of humans must state in the text that informed consent to publication was obtained from the patient or guardian. Authors should submit copies of written informed consents by using the online manuscript submission system. If it is unavailable, the IRB approval should be needed. Copy of IRB approval should be kept. If necessary, the editor or reviewers may request copies of these documents. Rarity of a disease condition is itself not an acceptable justification for a case report.

(1) Title page: Same as clinical and experimental studies.

(2) Manuscript

Title and Running title.

Abstract: All case reports should contain a structured abstract that is written only in English. Provide an abstract of no more than 150 words. It should contain 3 subsections: Background, Case, and Conclusions. A list of keywords, with a minimum of 6 and maximum of 10 items, should be included at the end of the abstract. The selection of keywords should be from MeSH (http://www.ncbi.nlm.nih.gov/mesh) and should be written in small alphabetic letters with the first letter in capital letter. Separate each word by a semicolon (;), and mark a period (.) at the end of the last word.

Introduction: Should not be separately divided. Briefly describe the case and background without a title.

Case report: Describe only the clinical statement that is directly related to diagnosis and anesthetic management.

Discussion: Briefly discuss the case, and state conclusions at the end of the case. Do not structure the conclusion section separately.

References: Do not exceed 15 references. For exceeding the number of references, it should be negotiated with the Edito-
3) Reviews
Review articles synthesize previously published material into an integrated presentation of our current understanding of a topic. Review articles should describe aspects of a topic in which scientific consensus exists, as well as aspects that remain controversial and are the subject of ongoing scientific disagreement and research. Review articles should include unstructured abstracts equal to or less than 250 words in English. Figures and tables should be provided in English. References should be obviously related to documents and should not be exceed 100. For exceeding the number of references, it should be negotiated with the Editorial Board. Body text should not exceed 30 A4 pages, and the number of figures and tables should be equal to or less than 6.

4) Letters to the Editor
Letters to the Editor also should include brief constructive comments on the articles published in KJA and interesting cases. Letters to the editor of humans must state in the text that informed consent to publication was obtained from the patient or guardian. Authors should submit copies of written informed consents by using the online manuscript submission system. If it is unavailable, the IRB approval should be kept. If necessary, the editor or reviewers may request copies of these documents. Letters to the Editor cover individual articles not described by any of the above categories. The short manuscripts with a constructive note on the Journal or the anesthesiology at large are welcome.

5) Book Reviews and Announcements
Book reviews as well as News of Scientific Societies and scientific meeting dates in Korea or abroad can be included. Their formats will be same as Letter to the Editor.

6) Statistical Round
A Statistical Round is a narrative review of the application of contemporary quantitative sciences to issues of concern to anesthesiology researchers. A Statistical Round involves a focused discussion on one or more unique or interesting statistical analysis methods that has previously been published in this journal or expresses the general policies or opinions of the Statistical Round Board. They are solicited by the Statistical Round Board and reviewed by the Statistical Editor. There are no word limits to or rules regarding the structure of a Statistical Round. They should have an unstructured abstract of no more than 250 words in English. All articles in a Statistical Round will be published in English and translated into Korean for the convenience of Korean readers. The Korean version of the Statistical Round will be published only on the Web page of the Journal (https://ekja.org). The inclusion of sample datasets as Web (Supplemental) content is encouraged.

8. Recently revised instructions for authors are applied from November 2019 submissions.