




Review

Intrathoracic Hemorrhage: Review of Thoracic Trauma Management in Civilian and Military Settings

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Abstract

Thoracic injuries requiring surgical intervention remain an important consideration in blunt and penetrating trauma with exceedingly high morbidity and mortality. In the United States, much of modern-day management of intrathoracic injuries has been derived from military medical experience. However, thoracic vascular injuries account for only 6% of thoracic trauma, leading to decreased preparedness to address such injuries. To address this knowledge gap, a literature review was conducted to examine the operative techniques for management of intrathoracic hemorrhage from direct cardiac injuries, great vessel injuries, and pulmonary injuries. A literature review was conducted via PubMed utilizing key terms “traumatic thoracic hemorrhage”, “traumatic cardiac injury”, “traumatic great vessel injury”, and “traumatic pulmonary injury”, “penetrating cardiac trauma”, “anterolateral thoracotomy”, “trauma extracorporeal membrane oxygenation (ECMO)”, “thoracic damage control surgery”, including studies from 1987 to present. Citation chaining and author discretion were also used to identify relevant articles for inclusion. Two primary operative approaches, the anterolateral thoracotomy and median sternotomy, provide adequate exposure to repair most intrathoracic injuries. Direct cardiac injuries are best repaired using permanent pledgeted sutures. Repair of traumatic great vessel injuries presents a significant challenge, often necessitating extension of the initial incision to enable proximal and distal vascular control when endovascular options are unavailable. Traumatic pulmonary injuries often require non-anatomic lung resection. Many aspects of care for intrathoracic hemorrhage in the civilian setting apply to battlefield management, however specific considerations such as availability of resources and patient transport are important in the context of potential for prolonged field care. In the future, there may be a role for venovenous and venoarterial extracorporeal membrane oxygenation. Algorithmic, flexible, and effective management considerations offer the greatest utility in management of high mortality injuries leading to intrathoracic hemorrhage in both civilian and military settings. New possible avenues for extracorporeal support in battlefield management offer additional approaches in care in the resource limited environment.

Keywords: intrathoracic hemorrhage; thoracic trauma; military

1. Introduction

Thoracic trauma is not uncommon in trauma patients. Thoracic injuries are found in 12–50% of civilian trauma patients [1]. The majority are due to a blunt mechanism and less than 10% require any surgical intervention. However, thoracic trauma as a whole presents a 9.4% overall mortality, 56% of which is in the first 24 hours after injury [2]. In conflicts in Iraq and Afghanistan, thoracic trauma was present in only 10.5% of battlefield injuries, however this was more likely to be due to a penetrating mechanism and was associated with a 10.5% mortality rate [3]. In the ongoing Ukraine-Russia conflict, thoracic injuries range between 28% to 52% of adult and pediatric patients [4,5]. See Table 1 for major differences in civilian and military thoracic trauma. Differences in mechanism may be related to confounding factors, such as body armor or armored vehi-

cles. In the military setting, the most common injuries identified in thoracic trauma include pneumothorax and pulmonary contusion at 51.8% and 50.2%, respectively, with the most common penetrating mechanism being a fragmentation injury from a blast at 84% [6]. Thoracic vascular injuries account for only 6% of thoracic trauma [2]. When surgical intervention is required in thoracic trauma patients, the overall mortality rate increases to 30% with stab wounds and 52% with gunshot wounds [7]. In this review, we examine direct cardiac injury, great vessel injury, and pulmonary injury as causes for intrathoracic hemorrhage requiring operative intervention, including a review of operative techniques and considerations for management in the forward deployed military setting.



Table 1. Differences in thoracic trauma injuries between civilian and military settings.

	Thoracic trauma characteristics	
Setting	Civilian	Military
Prevalence	12–50%	10.5%
Mortality	9.4%	10.5%
Most common mechanism	Blunt trauma	Penetrating trauma
Diagnostics	CXR, eFAST, CT/CTA	CXR, eFAST
Surgical approach	Anterolateral thoracotomy, median sternotomy, VATS, endovascular	Anterolateral thoracotomy, median sternotomy

eFAST, extended focused assessment sonography in trauma; CXR, chest x ray; CT, computed tomography; CTA, computed tomography angiogram; VATS, Video-Assisted Thoroscopic Surgery.

2. Materials and Methods

A literature review was conducted using PubMed. Key words searched included “thoracic hemorrhage”, “traumatic cardiac injury”, “traumatic great vessel injury”, “traumatic pulmonary injury”, “penetrating cardiac trauma”, “anterolateral thoracotomy”, “trauma ECMO”, “thoracic damage control surgery”. Studies included were those in English, with specific focus on those related to intrathoracic hemorrhage in the setting of thoracic trauma that included discussion of surgical intervention. The date range included papers from 1987 to present with a total of 69 studies reviewed. Additional literature sources were included based on the authors’ experience, as well as resources related to United States military medical guidelines on thoracic trauma.

3. Results

3.1 Initial Evaluation

Whether deployed or stateside, the initial evaluation with primary survey focuses on immediate life-threatening pathology [8]. Compared to the traditional teaching of “Airway Breathing Circulation”, there has been a recent transition towards “X-ABC”, or evaluation for exsanguinating hemorrhage prior to assessment of the patient’s airway, breathing, and circulation [9]. Given the high likelihood for hemodynamic instability in intrathoracic hemorrhage, considerations should be made to intubate in the operating room to decrease the delay to obtaining source control unless evidence of critical hypoxia is present [9]. After completion of the primary survey, the evaluation proceeds with adjuncts to primary survey of plain radiographs and ultrasound, specifically the Focused Assessment for the Sonography of Trauma (FAST) exam followed by secondary survey to assess additional injuries [5]. Of note in thoracic trauma, tube thoracostomy can often become a vital diagnostic tool when a hemothorax is identified. Although there are no significant differences in drainage failure or mortality, larger diameter thoracostomy tubes are associated with larger initial drainage volumes and shorter tube duration [10–15]. Traditional teaching states that chest tube output of 1500 cc at initial placement or >200 cc/hour necessi-

tates operative intervention [16]. In the setting of hemodynamic instability necessitating operative intervention, maximal exposure must be obtained to allow access to all necessary areas of possible injury, which traditionally includes sterile preparation from neck to knees in the supine position [17]. This holds true for thoracic hemorrhage as well. After making the determination that immediate operative intervention is indicated, there are two main approaches to intrathoracic hemorrhage: the anterolateral thoracotomy and median sternotomy.

3.2 Approaches

The anterolateral thoracotomy and the median sternotomy are the two surgical approaches that provide the most versatile exposure in thoracic trauma (see Table 2 for comparison between approaches). The anterolateral thoracotomy offers rapid access and sufficient visualization of many thoracic injuries. Traditionally completed on the left side in the 5th interspace, this incision can allow for visualization of the anterior apex of the heart, descending thoracic aorta, and left lung [18,19]. After initial incision with a scalpel, electrocautery or heavy mayo scissors can be used to divide underlying tissues, such as the pectoralis major, serratus anterior, and intercostal muscles. If time and clinical status permits, a muscle sparing approach may be used for the pectoralis major and serratus anterior [17]. The key maneuvers when performing this incision include starting the incision in the correct interspace, however if unsure on correct interspace, aim for a higher level than expected and carrying the dissection as far laterally as possible. Key pitfalls include making the incision too small and not accounting for the internal mammary artery, which must be ligated and divided as part of the incision, otherwise will account for significant bleeding into the field. Another key pitfall to avoid is injury to the phrenic nerve when opening the pericardium, which runs on the anterolateral surface of the pericardium. If there are any concerns related to traumatic pathology in the right chest after performing the left anterolateral thoracotomy, the incision can be extended across to the right side of the chest in a similar fashion, known as a clamshell thoracotomy [17,20]. Although not the primary focus of this review, the anterolateral thoracotomy can be

Table 2. Comparison overview between the two primary thoracic trauma approaches: anterolateral thoracotomy and median sternotomy.

Open thoracic trauma surgery approaches		
	Anterolateral thoracotomy	Median sternotomy
Indications	Massive hemothorax, pericardial fluid on eFAST (unstable patient), unilateral thoracic injury, witnessed traumatic cardiac arrest	Mediastinal trauma, pericardial fluid on eFAST (stable patient), suspicion of direct cardiac injury, hemorrhage from pericardial window
Target anatomy	Lung, descending aorta, anterior apex of heart, diaphragm	Heart, aortic arch, proximal great vessels, trachea, proximal bronchi
Extension	Clamshell thoracotomy	Trap door incision, supraclavicular incision, sternocleidomastoid incision
Advantages	Rapid access	Central exposure, versatility
Pitfalls	Inadequate incision, damage to mammary artery and/or phrenic nerve	Incision off midline, sternal saw related vascular injury, excessive osseous cautery

used in the setting of traumatic arrest, known as a resuscitative or emergency thoracotomy. The indications for thoracotomy in the setting of cardiac arrest in a trauma patient are variable in the guidelines, however the guiding principle includes pursuit of this maximally invasive technique if there is chance for reversible or treatable pathology [20]. Despite improved access to the thoracic cavity in the elective setting, a posterolateral thoracotomy is seldom used in trauma and would often require supreme evidence that no other traumatic pathology exists due to the difficulties accessing other body cavities from the required lateral decubitus positioning required for a posterolateral thoracotomy [20,21].

If concerned about direct injury to the heart of proximal great vessels, a median sternotomy offers another versatile approach [19]. A pericardial window may be used for further diagnostic evaluation, which if positive, would then progress to a sternotomy. After making an initial skin incision extended from the suprasternal notch down below the xiphoid, the overlying soft tissue is divided to expose the sternum. The space between the sternum and heart can be created bluntly. Once the sternum is divided, bone wax or high coagulation settings on electrocautery can be used to obtain hemostasis. Sternal retractors are then inserted, allowing full exposure of the anterior aspect of the pericardium in the midline. The key maneuver includes staying in the midline of the sternum. A sternotomy allows for exposure and treatment of injuries to the heart, aortic arch, and proximal great vessels with the exception of the left subclavian artery, however if the clinical situation necessitates, an anterolateral thoracotomy can be performed in conjunction with sternotomy, known as the trapdoor incision [20].

Minimally invasive techniques, specifically video assisted thoracoscopic surgery (VATS), are worth consideration as another method of surgical approach in thoracic trauma, however with specific limitations. Yu *et al.* [22] presents a series of cases of penetrating thoracic trauma involving pulmonary parenchyma injuries utilizing minimally invasive techniques, which may be a valuable resource specifically in the setting of hemodynamic stabil-

ity. Duggan *et al.* [23] also addressed the utility of VATS in diaphragm injuries, hemopericardium, and rib plating in the setting of rib fractures. Despite possible benefits, patients undergoing a VATS approach necessitate hemodynamic stability or preoperative computed tomography (CT) imaging as part of inclusion criteria, as employed by Akkas *et al.* [24] and Divisi *et al.* [25], respectively. Both factors may not be applicable for intrathoracic hemorrhage in the battlefield scenario, especially in the forward surgical environment without CT imaging capabilities or equipment required to complete a VATS procedure. In the Ukraine-Russia conflict, VATS was utilized in 36 patients sustaining thoracoabdominal penetrating trauma, in which 10 (28%) involved removal of metal fragments in a Role 2 hospital. In this series, 34 patients (96%) presented as hemodynamically stable and the majority of patients (20, 56%) underwent both thoracotomy and laparotomy. However, it is unclear the exact indication for progression to thoracotomy after the minimally invasive approach [26]. VATS' role in initial thoracic trauma management will likely continue to evolve in the civilian realm, however implementation in military thoracic trauma may be limited to stable patients with equipment readily available.

3.3 Direct Cardiac Injury

Direct injury to the heart is often seen in penetrating injuries and can be seen in both injuries directly to the thoracic cavity as well as injuries to the upper abdomen that have a trajectory into the chest. This injury pattern may present as cardiac tamponade with blood in the pericardium, however the absence of blood in the pericardium does not rule out a direct cardiac injury as blood could be draining into the pleural space [27]. The associated overall survival rate is low at 19%, therefore swift and effective decision-making is required with efficient determination that surgical intervention is required [28]. After completing an anterolateral thoracotomy or sternotomy, cardiac tamponade may be visualized and resolved by incising the pericardium to identify the underlying injury. Initial hemorrhage control

may be obtained by applying digital pressure over the site [12]. While maintaining direct pressure, a thorough survey of the potentially injured anatomy is prudent, taking into specific consideration the location of the injury with respect to coronary arteries and which chamber of the heart may be affected [14]. Generally, repair is performed with a series of 4-0 polypropylene sutures with or without pledgets, usually in a horizontal mattress repair [29]. Pledgets are often used with thin-walled chambers but may not be required for thick myocardium. It is imperative to ensure that no damage to a coronary vessel is made with the repair, especially given that cardiopulmonary bypass resources may be limited. If the injury is in close proximity to a coronary vessel, a horizontal mattress can still be used while taking great care to avoid damage to the vessel, especially given that cardiopulmonary bypass resources may be limited [30]. Another option for repair includes utilization of a pericardial patch over the defect [31]. With large lacerations, the patient may be at risk for air embolism, which often proves to be fatal. In this instance, place the patient in Trendelenburg and aspirate from the left ventricle to remove the air [15]. Complex cardiac injuries including injury to the coronary arteries or valves offer a significant challenge in the setting of trauma, which may need to be repaired at a later date after initial management of acutely life-threatening cardiac pathology [32].

3.4 Great Vessel Injury

Traumatic injury to the great vessels presents a unique challenge in the setting of intrathoracic hemorrhage. After appropriate preoperative evaluation, median sternotomy should serve as the initial incision if concerned for proximal great vessels or proximal aortic arch, while left thoracotomy is appropriate for injuries to the left subclavian or descending aorta. Following initial incision, surgical exploration with identification of the injured vessel becomes imperative. Once the injury is identified, the primary goal is to obtain proximal and distal control, which may require extensions of the initial incision. For the brachiocephalic artery, extension into a supraclavicular incision may be indicated. The left common carotid artery may require extension to a left anterior sternocleidomastoid incision. The classic difficult injury in the thoracic cavity is the left subclavian injury, which may be best approached with the addition of a left anterolateral thoracotomy in the 2nd interspace; the “trapdoor” incision. Vascular control can be obtained using vessel loops and non-crushing vascular clamps [33]. After vascular control, the degree of injury will determine the necessary repair. If amenable, primary end-to-end repair after debridement and embolectomy is an effective strategy. If a larger segment of the vessel is damaged, resection followed by venous interposition or synthetic graft reconstruction would be required [33]. Ligation of the carotid artery is generally not advised given the neurologic risk, however, it may be necessary in the setting of severe instability [34].

In the setting of blunt injury to the aorta, the management is related to degree of injury. Grade I refers to intimal disruption, Grade II intramural hematoma, Grade III pseudoaneurysm, and Grade IV aortic rupture. These are often diagnosed via CT imaging, provided the patient is able to obtain imaging as part of the trauma evaluation [35]. If in the setting of acute intrathoracic hemorrhage, this likely refers to a grade IV aortic injury, which is often fatal in the prehospital setting [36]. If resources allow, Grades II–IV are often best repaired from an endovascular approach, specifically thoracic endovascular aortic repair (TEVAR), however a patient-centered approach is required with some instances necessitating open repair [37,38]. Considerations regarding timing of repair are vital, as delayed repair (>24 hours) may be feasible to allow for the management of coexisting injuries with appropriate anti-impulse therapy [39]. Penetrating thoracic aortic injuries, specifically injury grades II–IV based on the review by Zambetti *et al.* [40], are also often best approached via an endovascular technique, however open repair for both blunt and penetrating trauma is an option, specifically with the use of an interposition graft with a “cut and sew technique” [40–42]. When compared to the endovascular approach, the open approach has significantly higher risks of mortality, spinal ischemia, and kidney injury [43,44].

Injuries to the great veins of the chest are uncommon in trauma. Lacerations or avulsions of the superior vena cava can be repaired with polypropylene suture in a running or interrupted fashion depending on the size of the injury [45,46]. Injuries to the azygous, hemi-azygous, or brachiocephalic veins can be ligated if the patient is in extremis [33,47,48]. Another uncommon cause for intrathoracic hemorrhage would be injury to the pulmonary artery, which would most likely present as a large hemothorax. Often rapidly fatal, however if the patient were to successfully make it to the operating room, management with direct pressure initially will control most bleeding. Proximal pulmonary artery lesions may require cardiopulmonary bypass and, depending on the degree of injury and resources available, pneumonectomy may be the only viable option for the patient [49].

3.5 Pulmonary Injury

Direct injury to the lung parenchyma leading to intrathoracic hemorrhage is best approached with an anterolateral thoracotomy with possible extension to clamshell thoracotomy if evaluation of the contralateral chest is required. With advances in technology and expertise, minimally invasive techniques, such as VATS can be employed in hemodynamically stable patients. In the setting of hemodynamic instability, open approaches are preferred. On initial entry, the chest should be packed in a systematic manner to not only control bleeding, but to then be able to be removed in a controlled manner to localize the site of hemorrhage. The standard maneuver for parenchymal injuries

involves a non-anatomic lung resection of the injured segment utilizing a gastrointestinal anastomosis (GIA) stapler with medium-thickness loads for most lung tissue [21]. Another option is to perform a tractotomy, in which multiple staple fires can be used to open the space between entrance and exit wounds to localize underlying bleeding vessels followed by approximation of the lung parenchyma, allowing for hemorrhage control without sacrificing lung parenchyma [21,50]. Smaller lacerations can be performed with suture repair, referred to as a pneumonorrhaphy, which often becomes the most common repair [51]. With increased complexity of resection required, the overall mortality increases. In situations of severe traumatic injury of the parenchyma and hilum of the lung, a trauma pneumonectomy may be required, which notably has a mortality rate at nearly 70% [51]. Such situations may lead to right-sided heart failure due to significant change in pulmonary vascular resistance, which leads to the possibly utility of extracorporeal membrane oxygenation (ECMO) in this setting [21].

4. Discussion

Several facets of trauma care in the civilian sector can be applied to the military, however there are certain aspects of military trauma care that are unique, often presenting new challenges that may not be present in civilian trauma. The most notable nuance is the severe resource limitation in military trauma care compared to major trauma centers. CT is often not available depending on level of care. Plain radiographs may be available, but there has been increasing utilization of ultrasound. Given these limitations, the extended focused assessment for the sonography of trauma (eFAST) has become pivotal for medicine in the austere environment [52]. Advanced modalities such as endovascular equipment for TEVAR and cardiopulmonary bypass would also be extremely limited, with only possible availability at the larger hospitals further from the site of initial injury. Although successfully implemented at the Role 2 level in the Ukraine-Russia conflict, VATS approaches require additional equipment that may not be feasible in the operational environment [26]. However, transport to a higher level of care may not be available due to operational constraints. VATS equipment in the forward operating theater may be necessary if medical teams are required to care for thoracic injuries for a longer duration prior to transfer, although this is contingent on battlespace resources and commander's intent.

Depending on both clinical status and operational standpoint, definitive repair of intrathoracic injuries may not be feasible, in which thoracic damage control procedures may be necessary. Traditional indications for damage control surgery of acidosis, hypothermia, and coagulopathy continue to apply, however considerations should also be made for type of injury, such as hilar injury, pneumonectomy, repair of vascular structures, or concomitant nontho-

racic injury requiring intervention [53]. This could include packing of the chest and placement of a temporary vacuum closure, or in the case of polytrauma, may take the form of a laparotomy and bilateral chest tubes prior to transfer to a higher level of care [20,54]. Although data regarding outcomes in thoracic damage control procedures is sparse, the review by Roberts *et al.* [55] indicated thoracic damage control procedures decreased need for anatomic lobectomy, shortened operative times, and reduced transfusion requirements, all which would be crucial in the battlefield environment. Deferring complex, time and resource-intensive repair may not only save the current casualty, but also save resources for future casualties and continue operational readiness.

The notion of "Golden Hour" of trauma care, referring to a trauma patient being evaluated by a surgeon within 1 hour of injury, was a principle followed closely in recent international conflict. As warfare continues to change, the expectations of the "Golden Hour" will likely evolve as well [56]. This constraint becomes especially difficult in the management of complex thoracic injuries that require transfer to a higher level of care; however the battlespace is not permitting. This is an instance highlighting the importance of prolonged field care, in which casualties need a higher level of care however are unable to reach that level [57]. In such resource-limited situations, especially when considering severe intrathoracic trauma, considerations arise regarding the utility of ECMO.

There are two primary forms of ECMO: venovenous (VV) and venoarterial (VA). VV configuration is traditionally used in severe pulmonary pathology without cardiac failure, such as acute hypoxemic respiratory failure or acute respiratory distress syndrome but can also be considered for anatomic injuries that require pneumonectomy [58]. This system functions via two venous cannulas; one to drain deoxygenated blood from the body and one to return after oxygenation via a membrane oxygenator [59]. VV ECMO primarily functions for gas exchange and therefore requires appropriate cardiac function [60]. This contrasts with VA configuration, which is primarily used in the setting of severe cardiogenic shock, allowing for both oxygenation of blood and perfusion of peripheral tissue [61]. The traditional set up involves drainage from a venous cannula, typically the femoral vein, and blood return via an arterial cannula, typically the common femoral artery [62]. This can allow for other lifesaving interventions to occur while maintaining both perfusion and oxygenation. Weaning from ECMO occurs in a systematic fashion after improvement from the offending agent, gradually decreasing ECMO support while increasing traditional ventilator strategies. This usually involves sequential decrease in fractional inspiratory oxygen (FiO₂), flow of the circuit, and gas flow, known as sweep [63]. In VA ECMO, additional weaning considerations should be made for assessment of cardiac function as liberation would require favorable evolution of myocar-

dial recovery [64]. Depending on the injury pattern, both VV and VA ECMO may have a role in intrathoracic hemorrhage.

ECMO implementation in the setting of intrathoracic hemorrhage does present a unique challenge. A major contraindication to ECMO is active hemorrhage [63,64]. This also coincides with bleeding as the most common complication at 27% regardless of type of ECMO [65]. The circuit itself is thrombogenic, additionally leading to clotting complications both in the patient and the circuit, necessitating anticoagulation [66]. Both of these factors would be at odds with ECMO utilization in the setting of intrathoracic hemorrhage, however novel low-dose anticoagulation protocols may allow for protection against thrombotic complications while decreasing bleeding risk [67].

Initial results of ECMO use in trauma are positive overall, although data is limited due to relatively low sample sizes and the overwhelming severity of injury for patients in which ECMO is applied. In the study by Zangbar *et al.* [68], utilization of VV ECMO in the setting of severe blunt thoracic injury was shown to have improved mortality, although no data related to intrathoracic hemorrhage pathology was delineated in this retrospective cohort. Currently, ECMO utilization in trauma is primarily in the setting of severe trauma-related cardiopulmonary failure, hemorrhagic shock, and cardiac arrest [69]. Applying these principles with the need for solutions with prolonged field care, ECMO could serve as a bridge where definitive thoracic injury repair is not feasible, but damage control procedures could be applied while maintaining perfusion via extracorporeal means. This is contingent on multiple factors, ranging from the role of anticoagulation needed for ECMO in a severely injured trauma patients to the technology and resources required to use a mobile ECMO unit [70,71]. The United States Military ECMO team based out of San Antonio Military Medical Center completed 110 ECMO transports from September 2012 to December 2019, primarily for acute respiratory failure (76.9%), with trauma as a factor in only 7.1%, and a median air transport distance was 1328 miles [72]. This not only highlights the significant resources required for ECMO, but the current reliance on air transport, which may not be available in the future battlespace. ECMO would require extensive technological advancements to enable front-line utilization on the future battlefield. Further investigation is needed on multiple fronts before pursuing this as a feasible solution, although there is certainly promise from a conceptual and initial data standpoint.

5. Conclusion

Intrathoracic hemorrhage presents a unique challenge in trauma care, presenting both the need for urgency of effective surgical intervention and utility of standardized, efficient decision making. Although rare in trauma today, patients sustaining direct cardiac injuries, great vessel injuries,

and pulmonary injuries that require immediate operative intervention pose one of the greatest mortality risks in trauma patients. Emphasis on reliable approaches and fundamental surgical technique can ensure effective management of both civilian and battlefield trauma patients.

Abbreviations

ECMO, extracorporeal membrane oxygenation; VATS, video-assisted thoracoscopic surgery.

Author Contributions

Conception and design: JA, GT, PM. Administrative support: GT. Provision of study materials or patients: BS, JK, EW. Collection and assembly of data: BS, JK, EW, RY. Data analysis and interpretation: BS, JK, EW. Manuscript writing: All authors. Manuscript editing: All authors. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest. Gregory D. Trachiotis is serving as one of the Editorial Board members of this journal. We declare that Gregory D. Trachiotis had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Hossein Shayan.

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