Int J Med Rev 2025 June;12(2): 901-912

10.30491/IJMR.2025.506302.1309

INTERNATIONAL JOURNAL OF MEDICAL REVIEWS

Narrative Review

Pathogenesis and Management of Bone Cement Implantation Syndrome: A Brief Review

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Received February 12, 2025; **Accepted** April 5, 2025; **Online Published** June 30, 2025

Abstract

Introduction: Bone cement implantation syndrome (BCIS) represents a potentially life-threatening complication of orthopaedic surgery. It poses a risk of intraoperative mortality and morbidity, particularly prevalent in cemented hip arthroplasty procedures. It can also present postoperatively in a milder form, leading to hypoxia and disorientation. With the increasing number of hip replacement surgeries, particularly among older adults, the risk of BCIS rises correspondingly.

Methods: In this literature review, we conducted a thorough, comprehensive search of academic databases. We identified relevant studies published in the last 8 years regarding BCIS following arthroplasty surgery.

Results: Twenty-two studies were identified. The studies suggested that people who have cemented hip hemiarthroplasty to fix a broken femur neck are more likely to experience BCIS. While severe BCIS is uncommon, it can be very serious, often resulting in death shortly after surgery or within 30 days. To prevent this, doctors should carefully assess patients before surgery, looking for risk factors like high ASA scores, chronic obstructive pulmonary disease (COPD), and medications like diuretics or blood thinners. More research is needed to improve treatment options for BCIS and better understand what causes it.

Conclusion: The full understanding of BCIS remains elusive. This article offers a review of BCIS, covering its definition, occurrence, risk factors, causes, mechanism, clinical symptoms, preventive measures, and treatment.

Keywords: Bone Cement, Arthroplasty, Hip, Postoperative Complications

Introduction

For over fifty years, bone cements have effectively secured artificial joints, including those in the hips, knees, shoulders, and elbows. Chemically, bone cement is essentially Plexiglas, also known as polymethyl methacrylate (PMMA), which was developed in the 1920s. PMMA has been utilized in various fields, ranging from serving as transparent glass alternatives in windows to applications in semiconductor research and even as material for the bodies of electric guitars. PMMA, commonly referred to as Plexiglas, was initially synthesized by Otto Röhm in 1902. It is a rigid material possessing glass-like characteristics and has found extensive utilization across various applications. The contemporary formulation of PMMA bone cements is credited to Degussa and Kulzer in 1943. They elucidated the polymerization process of methyl methacrylate (MMA) at ambient temperature, employing a co-initiator, typically a tertiary aromatic amine. Renowned English surgeon Sir John Charnley is often acknowledged for pioneering the use of bone cement in orthopaedic procedures. Drawing upon his background in dentistry, he initially utilized dental acrylics for attaching prostheses in total hip replacement (THR) surgeries. Subsequently, in 1965, he transitioned to specialized bone cement tailored for orthopaedic applications, marking a significant advancement in orthopaedic surgery.[1-6]

Regulatory approval for the use of bone cement in the fixation of hip and knee prostheses was granted by the FDA in the 1970s. PMMA, an abbreviation for polymethyl methacrylate, constitutes an acrylic polymer composed of two sterile constituents: a liquid monomer known as methyl methacrylate and a powdered co-polymer containing MMA and styrene. Upon amalga mation, the liquid monomer initiates polymerization around the pre-polymerized powder particles, resulting

in the formation of solidified PMMA. This process generates heat due to its exothermic nature. To introduce antibiotics, they can be incorporated into the polymerized matrix as a soluble powder, subsequently released into the joint cavity. Qin et al. documented a case where the use of antibiotics-loaded bone cement contributed to the occurrence of bone cement implantation syndrome (BCIS) by encasing the surface of the diseased bone. Hence, bone cement serves as a contemporary vehicle for drug delivery, facilitating the direct adminis tration of essential pharmaceuticals to the surgical site. Additionally, a contrast agent, typically zirconium dioxide (ZrO_2) or barium sulphate ($BaSO_4$), is integrated into the cement to enhance its visibility on radiographs. Further enhancements explored for bone cement encompass silver-containing nanoparticles endowed with antibacterial properties, bacteriocins as substitutes for antibiotics, and vitamin E, which exhibits favourable effects on mitigating free radical oxidation and exothermic activity.[2,7]

Artificial hip joints are frequently secured using bone cement due to the substantial forces they endure —approximately 10-12 times the body weight. The purpose is to ensure the long-term stability of the artificial implant by absorbing these forces. Despite its name, "cement", which typically denotes a substance that bonds materials together, PMMA functions more as a space-filling agent, creating a snug fit that secures the implant against the bone, akin to a "grout". Rather than possessing adhesive properties, bone cement relies on a mechanical interlock between the prosthesis and the irregular bone surface. Millions of such procedures are performed globally each year, with over half of them routinely employing bone cements—a number that continues to rise. Bone cement is valued for its reliability in anchoring implants, its straightforward application in clinical settings, and its proven durability with cemented prostheses. Evidence from hip and knee replacement registries in countries like Sweden and Norway underscores the benefits of cemented prostheses. Furthermore, guidelines from NICE advocate for cemented implants over uncemented ones in hip fracture management for adults, citing advantages such as improved postoperative mobility without pain and reduced re-operation risks.[3,4]

In the early 1970s, there was a notable increase in case reports linking intraoperative deaths to cementation and the insertion of prostheses. Fatal outcomes, attributed to air and fat embolisms, were documented in patients undergoing procedures involving bone cement, particularly in conjunction with hip replacement surgeries. Symptoms observed varied widely, but common manifestations included hypoxia, hypotension, cardiac arrhythmias, loss of consciousness, and cardiac arrest. The term "Bone Cementation Implantation Syndrome (BCIS)" emerged during this period and is now widely accepted in the medical community. BCIS is a complication observed following the implantation of PMMA during surgical procedures, significantly impacting both mortality and morbidity rates. While BCIS is commonly associated with patients undergoing cemented hip hemiarthroplasty, it can also manifest in individuals undergoing various other arthroplasty procedures, including total hip and knee replacements. It is noteworthy that BCIS may present with varying degrees of severity during the postoperative period. Documented in numerous published studies, BCIS has been observed to occur during specific phases of surgery, which include femoral reaming, acetabular or femoral cementation, prosthesis insertion, joint reduction, and, infrequently, limb tourniquet deflation in patients undergoing cemented arthroplasty. Despite lacking a universally accepted definition and full understanding, the syndrome exhibits clinical features predominantly marked by indicators such as diminished oxygen levels, systemic hypotension, pulmonary hypertension, erratic cardiac rhythms, syncope, and the potential for cardiac arrest. In 2009, Donaldson et al. introduced a standardized description of BCIS, focusing primarily on its cardinal symptoms. BCIS is defined as a condition typified by hypoxia, hypotension, or both, accompanied by sudden loss of consciousness occurring during the cementation and implantation of a prosthesis. Additionally, they proposed a grading system to evaluate the severity of hypoxia, hypotension, syncope, and cardiovascular collapse.[1,6,8-10]

At present, there is not a lot of consensuses about the standardized delineation of BCIS. The actual prevalence of fatal consequences linked to BCIS is uncertain due to inconsistent reporting of BCIS-related mortality, and instances with milder BCIS are often not adequately documented. However, recent studies have begun to explore its occurrence in patients undergoing various arthroplasty procedures. In a 2020 retrospective observational study by Rassir et al., they examined the incidence of BCIS among 3294 patients undergoing

Table 1. Severity Score of BCIS.

	Grade 1	Grade 2	
SpO_2	< 94%	<88%	
SAP	20% drop	40 % drop	
Other		Unexpected loss of consciousness	Cardiovascular collapse requiring CPR

SpO_2, oxygen saturation; SAP, systolic arterial pressure; CPR, cardiopulmonary resuscitation.[4,6]

cemented arthroplasties for various indications. They found an overall BCIS incidence of 26% across all included arthroplasties. Specifically, the incidence was 31% in hip hemiarthroplasty (282 out of 915), 24% in total hip arthroplasty (165 out of 677), 28% in total knee arthroplasty (210 out of 765), 20% in unicondylar knee arthroplasty (113 out of 558), 23% in revision arthroplasty (47 out of 206), and 16% in shoulder arthroplasty (28 out of 173).[6,9,10]

The recorded incidence of death following cemented total hip arthroplasty surgery fluctuates, with an approximate rate of 0.11%, mostly concentrated during the cementation phase. Parvizi et al. attributed all surgical fatalities to the use of bone cement, providing evidence of fatality rates of 0.16% for cemented total hip arthroplasty and 0.4% for cemented hip hemiarthro plasty. The likelihood of mortality after surgical procedures seems to be positively associated with the severity of the fracture and certain pre-existing conditions, such as pathological fractures. For patients who had cemented hemiarthroplasty for pathological fractures, the death rate during surgery was 4.3%. On the other hand, for patients who required bone cement and long-stem components in their procedures, the mortality rate was 1%. An analysis was conducted on a group of 1016 individuals who had cemented hemiar throplasty for femoral fractures. The study found that the total incidence of BCIS was 28%. The incidence rates of BCIS grades 1, 2, and 3 were documented as 21.0%, 5.1%, and 1.7%, respectively. Weingärtner et al. performed a retrospective observational study to investigate the occurrence of BCIS in 208 patients who had cemented hemiarthroplasty for proximal femur fractures. The research revealed that 37% of the patients had signs of BCIS.[10-17]

The clinical manifestations of BCIS exhibit a broad range of severity, ranging from mild to severe. The majority of individuals affected experience a mild form of BCIS, marked by transient episodes of hypotension and hypoxia, alongside cardiac arrhythmias that lead to a notable but temporary decrease in arterial oxygen saturation and systolic blood pressure (SBP) during the peri-cementation period. However, a minority of patients may progress to severe BCIS, characterized by significant intraoperative cardiovascular alterations that can lead to arrhythmias, shock, or cardiac arrest. The majority of studies relate these alterations to the occurrence of right ventricular failure, which is caused by an elevation in pulmonary vascular resistance (PVR). The increase in afterload causes the expansion of the thin-walled right ventricle, resulting in the displacement of the interventricular septum towards the left. As a consequence, there is a decline in the flexibility of the left ventricle, leading to a reduction in the amount of blood it can hold and the amount of blood pumped out with each heartbeat (cardiac output). The exact causes of the increased PVR are still uncertain, maybe resulting from the systemic absorption of the volatile monomer or the accumulation of cement or fat emboli. The presence of clinical manifestations of BCIS, together with a quick decrease in end-tidal CO_2 ($ETCO_2$) levels, are very reliable indications. However, a conclusive diagnosis usually requires a computed tomographic (CT) scan.[6,17]

Pathogenesis

The exact causes and mechanisms underlying BCIS are not completely understood, and various theories have been suggested and explored. One of the initial theories centred on the release of MMA into the bloodstream and its potential toxicity. Recent studies have put forward alternative explanations, including mechanisms related to an elevated pulmonary embolic burden resulting from high intramedullary pressure, along with other factors such as mediator release and complement activation triggered by cementation and prosthesis insertion.

Monomer-Mediated Model

Earlier research describing the vasodilatory impact of MMA, resulting in the relaxation of vascular smooth muscles and an increase in coronary blood flow.

Additionally, MMA exhibits direct toxicity towards the respiratory system, skin, and eyes. However, this theory was only supported by in vitro studies. In vivo, several animal studies have revealed that the plasma concentrations of MMA following cemented hip arthroplasty are below the threshold required to trigger pulmonary and haemodynamic deterioration. Consequently, subsequent studies have shifted their focus towards the embolic model as they seek to elucidate the pathophysiology of BCIS.[4,6,11,12]

Embolus-Mediated Model

Recent studies have been examining, both postmortem and using echocardiography, the impact of embolization in BCIS. Using echocardiography, researchers have detected embolic showers in various areas, including the right atrium, RV (right ventricle), and pulmonary artery during surgical procedures. Post-mortem investigations have confirmed pulmonary embolization in both animals and humans. The physiological effects of embolization are believed to stem from both mechanical factors and the release of mediators, leading to heightened pulmonary vascular tone. Research has shown that the debris causing embolization includes substances such as fat, marrow, cement particles, air, bone particles, and aggregates of platelets and fibrin. The pathological process is shown in the picture.[4,6,16,18]

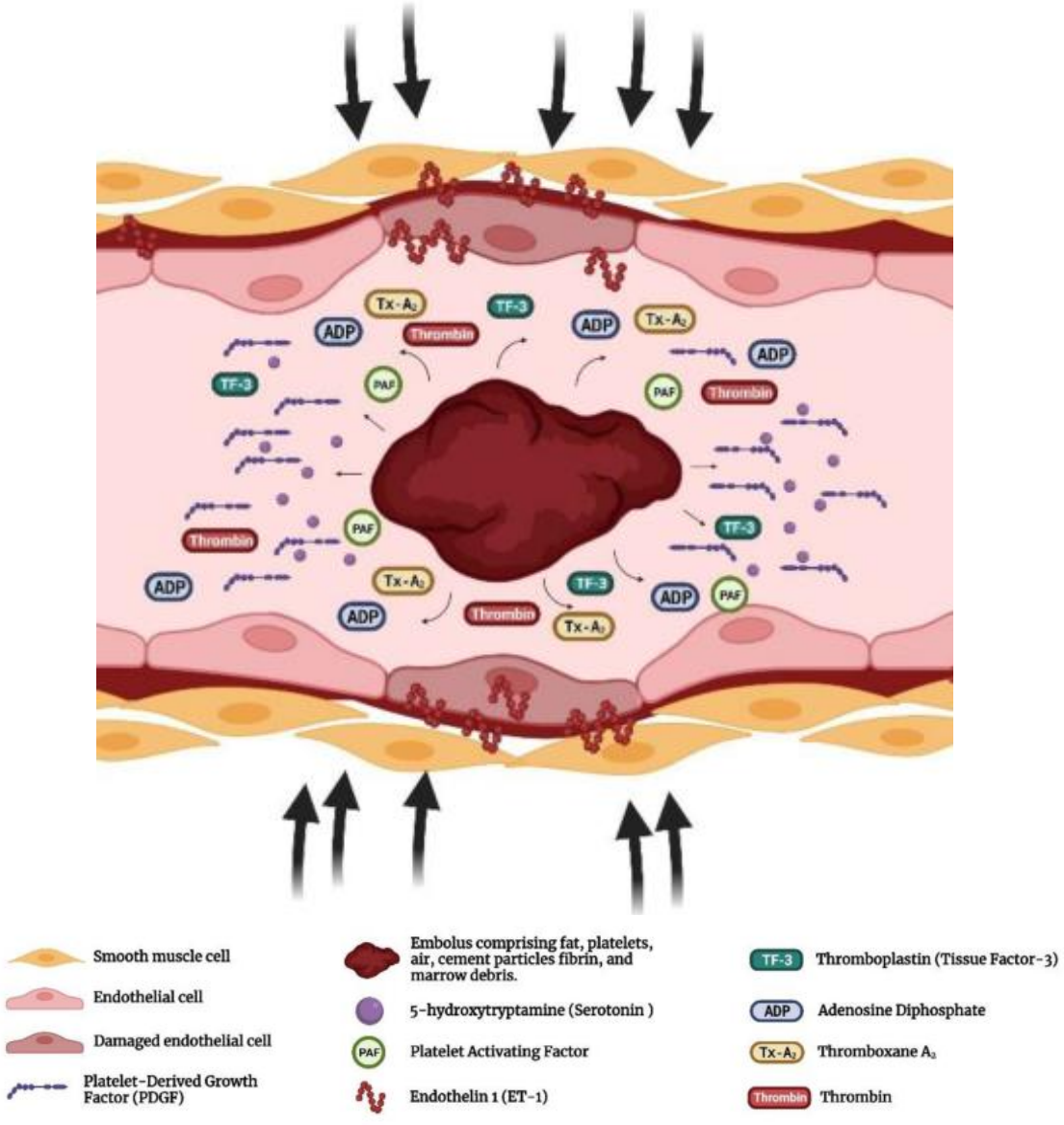

Figure 1. A Pulmonary Vessel Obstructed by an Embolus Composed of Fat, Platelets, Fibrin, and Marrow Debris. The consequences of such an embolus may stem from mechanical factors, the release of mediators, or a combination of both.[6]

During surgical operations, echocardiographic scans have detected emboli in the right atrium, right ventricle, and pulmonary artery. The emboli have been shown to include a variety of components, including fat, marrow, air, bone particles, cement particles, and aggregates of platelets and fibrin. The effects of these emboli are thought to be induced by mechanical causes, the release of mediators, or a mix of both. Embolization happens as a result of increased pressure inside the bone marrow during the process of cementation and the placement of prostheses. This process is ascribed to the exothermic reaction of the cement, resulting in its expansion inside the gap between the prosthesis and bone. Consequently, air and medullary contents are trapped and then forcefully pushed into the circulation. The temperature of the cement may reach a maximum of 96 °C within 6 minutes after its components are mixed. Emboli not only physically obstruct the pulmonary vasculature but also contribute to an elevation in pulmonary vascular resistance (PVR) via other means. At first, emboli may harm the endothelium, which triggers the release of endothelin factor-1 from the endothelium of pulmonary arteries, resulting in vasoconstriction. Alternatively, they may mechanically stimulate the blood vessels in the lungs, causing an automatic narrowing of the blood vessels. In addition, it is theorized that the embolic particles may release substances that cause blood vessels to constrict or become inflamed, such as thrombin and tissue thromboplastin. This might directly increase pulmonary vascular resistance (PVR) or indirectly trigger the release of other substances that further raise PVR. Embolism causing blockage in the pulmonary arteries and the subsequent constriction of these vessels by mediators lead to a mismatch between ventilation and perfusion (V/Q) and the development of hypoxaemia. Additional mediators, such as 6-keto PGF 1α and tissue thromboplastin, cause a decrease in systemic vascular resistance (SVR) by stimulating the release of secondary mediators such as adenine nucleotides. The elevated pulmonary vascular resistance (PVR) combined with the reduced preload of the right ventricle caused by the decrease in systemic vascular resistance (SVR) leads to a substantial decline in cardiac output (CO), which worsens hypotension. Pre-cement insertion medullary lavage effectively reduces the release of some mediators. [4,6,13,18,19]

Several researchers have used transesophageal echocardiography (TOE) to detect emboli within the heart, which exhibit considerable variation in size and quantity (Figure 1). In one instance, these emboli were reported to reach lengths of up to 5 cm. A study involving 48 patients undergoing cemented arthroplasty revealed emboli in 47 of the patients. The authors described the appearance of numerous small emboli as resembling a "snow flurry". Approximately one-third of the participants in the study exhibited detectable emboli larger than 10 mm. TOE findings indicate a higher incidence of emboli following cemented hip arthroplasty compared to uncemented procedures. This observation was corroborated by a small study involving seven patients who underwent complete hip arthroplasties, both cemented and uncemented. Throughout the entirety of the surgical procedure, "snow flurries" were occasionally observed on TOE, particularly in the cemented group during femur and acetabulum reaming, as well as during femoral component insertion and hip joint reduction. Interestingly, there was no notable increase in the frequency or length of these flurries at any specific point during uncemented arthroplasty procedures. Minimal changes in cardiores piratory variables were noted during these occurrences. In a study involving canines, both cemented and uncemented arthroplasty patients were found to have fat and marrow present in their pulmonary micro vasculature upon post-mortem examination. Comparatively, dogs that underwent cemented procedures exhibited a nearly tenfold increase in observed emboli during autopsy, as opposed to those in the uncemented group.[13,15,16]

Following intraoperative fatalities during cemented arthroplasty, post-mortem examinations are conducted to detect the presence of MMA microparticles, bone emboli, fat, marrow, and other substances in the lungs. Additionally, fat emboli have been identified in the brain, kidneys, and myocardium of a patient who suffered cardiac arrest while undergoing femoral prosthesis insertion post-mortem. In the context of a cemented prosthesis, pressure is intentionally applied to force the cement into the bone voids, thereby enhancing the bond between the cement and bone through increased contact surface area. Uncemented arthroplasty is associated with milder haemodynamic changes, fewer emboli, and lower intramedullary pressure.[16-20]

The level of embolization may be influenced by the

peak pressure generated in the femoral canal. In a study, both cemented and uncemented surrogate femoral prostheses were implanted into anaesthetized dogs to investigate emboli development mechanics. The cemented group demonstrated significantly higher peak intramedullary pressure and a higher frequency of pulmonary emboli observed during post-mortem examination. Even when bone wax, instead of cement, was used to create elevated intramedullary pressures using a non-volatile material in the femur, the observed cardiovascular alterations and embolic burden were still notably greater than those observed in the uncemented group.[1,4,6,21]

The debris from the medulla can affect various body systems, including the lungs, heart, and, para doxically, the cerebral and coronary circulations. It's suggested that showers of pulmonary embolisms may lead to right ventricular dysfunction and hypoxia, subsequently resulting in hypotension. Research suggests that the severity of cardiovascular dysfunction may not always correlate with the extent of embolic burden. The embolic model is widely acknowledged as the primary explanation for the causal mechanism in BCIS. However, it does not fully account for all reported events. Embolization does not consistently result in changes in blood flow, and the severity of embolism is not strongly correlated with low blood pressure or low oxygen levels. Studies utilizing Trans esophageal Echocardiography (TOE) have revealed frequent embolic events, with the majority of individuals showing good tolerance towards them. Researchers found that the emboli were smaller in size than the diameter of functioning pulmonary gas exchange channels, measuring 75 mm compared to 150 mm. The authors speculated that these tiny emboli would become lodged in the terminal pulmonary arteries, while the larger vessels supplying functioning gas exchange units would remain unaffected, thereby preserving a normal ventilation-perfusion (V/Q) ratio. However, they were unable to demonstrate V/Q mismatching 30 minutes after femoral prosthesis insertion. Hypotension has been observed in patients receiving MMA cement during procedures such as percutaneous vertebroplasty, even when the likelihood of severe embolism is low. While micro-embolism may play a role in BCIS, it is likely that additional processes are also involved.[9,10,15,22]

Histamine Release and Hypersensitivity

The histamine release mechanism in BCIS is not mutually exclusive from the embolic model; rather, it may act synergistically to worsen the haemodynamic and respiratory consequences of embolization. During cementation, embolic material—such as fat, bone marrow, air, and cement particles—enters the circulation and obstructs the pulmonary vasculature, leading to increased pulmonary vascular resistance, elevated right heart pressure, and impaired gas exchange. In 1972, anaphylaxis, which is a type 1 hypersensitivity reaction, was suggested as a possible cause for a fatal instance of BCIS. Anaphylaxis and BCIS have several overlapping clinical characteristics. Empirical research has shown a significant rise in histamine concentrations in the blood plasma of persons undergoing cementation operations who also had low blood pressure. The exact reason forthis histamine release is still unknown, since it is uncertain whether it is triggered by direct contact with the cement monomer or by an IgE-mediated mechanism. research found that the administration of clemastine and cimetidine, which are H1 and H2 antagonists, respectively, had a protective effect via blocking histamine receptors. Nevertheless, these effects have not been reliably replicated in more subsequent studies. Surgeons and experimental animals have been reported to have contact hypersensitivity, especially Type 4 hypersensitivity, to MMA.[4,17,20]

Multimodal Model

The pathogenesis of BCIS involves a multimodal interaction of mechanical, chemical, and physiological processes, each contributing to the haemodynamic and systemic effects observed during cemented arthroplasty. These processes often occur simultaneously and are influenced by individual patient factors, including baseline cardiac and pulmonary function, comorbidities, and intraoperative variables.

A significant mechanical component of BCIS is the embolization of intramedullary contents. During the pressurization of polymethylmethacrylate (PMMA) bone cement, fat, marrow, air, and other debris are forced into the venous circulation. These emboli travel to the pulmonary vasculature, causing mechanical obstruction that increases pulmonary vascular resistance (PVR). The sudden rise in PVR places considerable strain on the right ventricle (RV), which must work harder to maintain cardiac output. In some cases, this

can lead to acute RV dysfunction, reduced left ventricular preload, and systemic hypotension. The risk of embolization depends on factors such as the cementing technique, prosthesis design, and the quality of the patient's bone. Fragile or osteoporotic bones are particularly susceptible to excessive intramedullary pressurization, increasing the likelihood of significant embolization.

Chemical toxicity also plays a crucial role in BCIS. During the exothermic polymerization of PMMA, monomers are released into the bloodstream and absorbed by vascular endothelium and myocardial tissue. These monomers may have direct toxic effects, impairing endothelial and myocardial function. Vascular endothelial damage increases permeability, potentially contributing to pulmonary oedema, while myocardial toxicity reduces contractility, further compromising cardiac output. Additionally, the exothermic reaction of PMMA can damage adjacent tissues, exacerbating the release of debris into circulation and amplifying the mechanical embolization process.

The release of vasoactive substances is another key factor in BCIS pathogenesis. Embolization and chemical triggers activate platelets and mast cells, leading to the systemic release of histamine, serotonin, and thromboxane A2. Histamine causes systemic vasodilation and increased vascular permeability, reducing systemic vascular resistance (SVR) and contributing to hypo tension. Meanwhile, serotonin and thromboxane A2 promote pulmonary vasoconstriction, further increasing PVR and exacerbating the strain on the RV. Bronchoconstriction caused by these mediators can also worsen hypoxaemia. The effects of vasoactive mediators vary between individuals, influenced by factors such as preoperative medications like morphine, which can enhance histamine sensitivity.

The interplay between pulmonary and cardiovascular systems is particularly important in the pathogenesis of BCIS. Increased PVR due to embolization and vasoactive mediator release places a sudden afterload on the RV, potentially leading to RV failure in patients with preexisting dysfunction. This reduces left ventricular preload and systemic perfusion, contributing to hypotension and reduced oxygen delivery to vital organs. Simultaneously, systemic vasodilation caused by histamine release lowers SVR, compounding the haemodynamic instability. Hypoxaemia resulting from ventilation-perfusion mismatch further compromises oxygenation, creating a cycle of worsening cardiac and pulmonary dysfunction.

Individual susceptibility to BCIS varies based on patient comorbidities and physiological reserve. Patients with preexisting cardiovascular conditions, such as pulmonary hypertension, ischemic heart disease, or chronic obstructive pulmonary disease (COPD), are particularly vulnerable. Compromised RV function limits the ability to accommodate the acute rise in PVR caused by embolization and pulmonary vasoconstriction. Similarly, systemic vasodilation and impaired myocardial function have a more pronounced impact on patients with limited cardiovascular reserve, such as elderly individuals or those with significant frailty. These factors highlight the importance of preoperative risk stratification and individualized intraoperative manage ment in reducing the incidence and severity of BCIS.

The haemodynamic changes associated with BCIS are the result of a dynamic interplay between increased PVR, decreased SVR, and impaired myocardial contractility. These factors do not act in isolation; rather, they interact synergistically to produce the clinical manifestations of BCIS. For example, embolization may initiate an inflammatory response that exacerbates pulmonary vasoconstriction, while monomer toxicity and systemic vasodilation further impair cardiac function. This complex interaction underscores the multifaceted nature of BCIS and the need for a comprehensive approach to its prevention and management (Figure 2).[4,6,8,19,23,24]

Management

BCIS grades 2 and 3 have demonstrated a notable perioperative mortality rate and are associated with a 16-fold increase in the likelihood of death within 30 days after surgery.[25,26] Recognizing the importance of devising strategies for preventing and effectively treating BCIS is crucial. In 2015, Griffith et al. introduced safety recommendations aimed at minimizing the potential risks of cemented hemiarthroplasty. These guidelines underscore the necessity of multidisciplinary clinical supervision during the perioperative period, involving the anaesthetist, surgeon, and orthogeriatrician.[14] Following a thorough assessment of the risk factors associated with frail patients undergoing hip hemiarthroplasty, the following conclusions were reached:

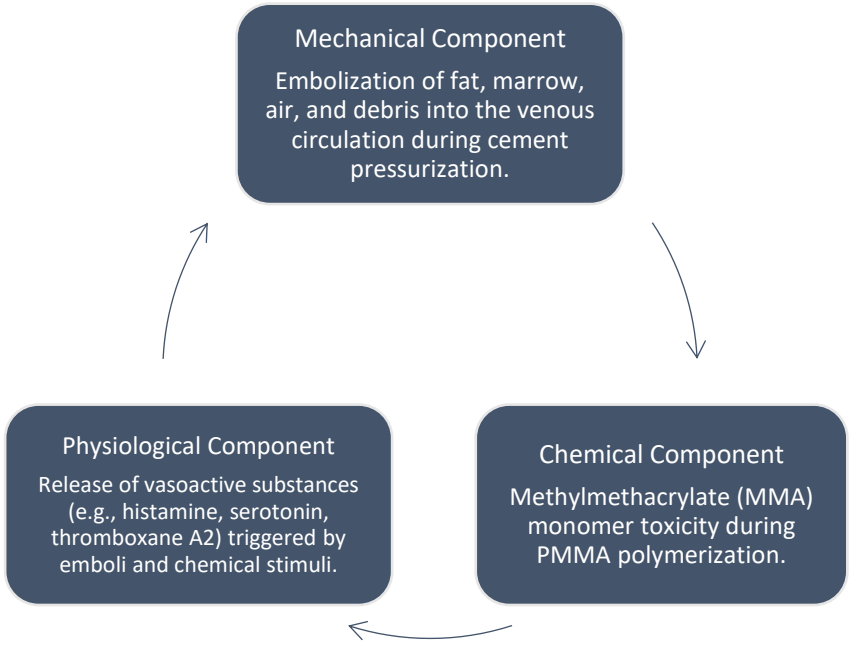

Figure 2. Synergistic Interaction of Individual Components to Produce the Clinical Manifestations of BCIS.

1. Surgeons, anaesthesiologists, and orthogeriatric specialists are deliberating on optimal strategies to mitigate the initial surgical risks associated with mortality and complications.
2. Surgeons and anaesthesiologists are advised to modify perioperative protocols to mitigate the occurrence of cardiovascular events and improve outcomes should such events occur.
3. All hip fracture surgeries should be conducted or closely supervised by appropriately qualified anaesthesiologists and surgeons.

Furthermore, the guidelines offer fundamental recommendations to surgeons and anaesthesiologists regarding the prevention and management of BCIS. Unfortunately, the current data on specific strategies for preventing and treating BCIS is insufficient. The principal aim of the procedure should be to reduce the probability of BCIS occurrence, especially among high-risk individuals. Table 2 outlines the pathological and surgical risk factors linked to BCIS development, as suggested by Hines et al. (1996). An orthopaedic surgeon well-versed in these factors plays a crucial role in BCIS treatment.[4,6,9,27,28]

Before cementation, surgical procedures should prioritize the removal of medullary contents and effectively reduce excessive intramedullary pressure. Animal studies have demonstrated that conducting high-volume, high-pressure pulsatile lavage of the intramedullary cavity after reaming can significantly mitigate alterations in pulmonary haemodynamics, PaO_2levels, and intrapulmonary shunt fraction (Qs/Q_t). While conclusive evidence in humans is lacking, medullary lavage is strongly recommended as an effective approach to reducing intramedullary contents before cementation. An alternative surgical strategy aimed at minimizing the volume of material introduced into the femoral canal involves the creation of venting apertures in the femur during cementation, facilitating the release of trapped air. However, this approach is associated with an elevated risk of femoral fracture. In contrast, employing retrograde cement insertion with a cement gun, despite inducing higher intramedullary pressure relative to finger-packing, results in a slower decline in oxygen saturation levels during cementation. The bone-vacuum cementing technique has been demonstrated to significantly diminish embolic burden during hip arthroplasty, as validated by intraoperative transoesophageal ultrasound assessment. Furthermore, the preparation of bone cement under partial vacuum conditions attenuates the rate of oxygen saturation decline during cementation compared to atmospheric pressure preparation. Additionally, the selection of prosthesis stem length plays a role in determining the incidence of cardiopulmonary complications.[19-21,29]

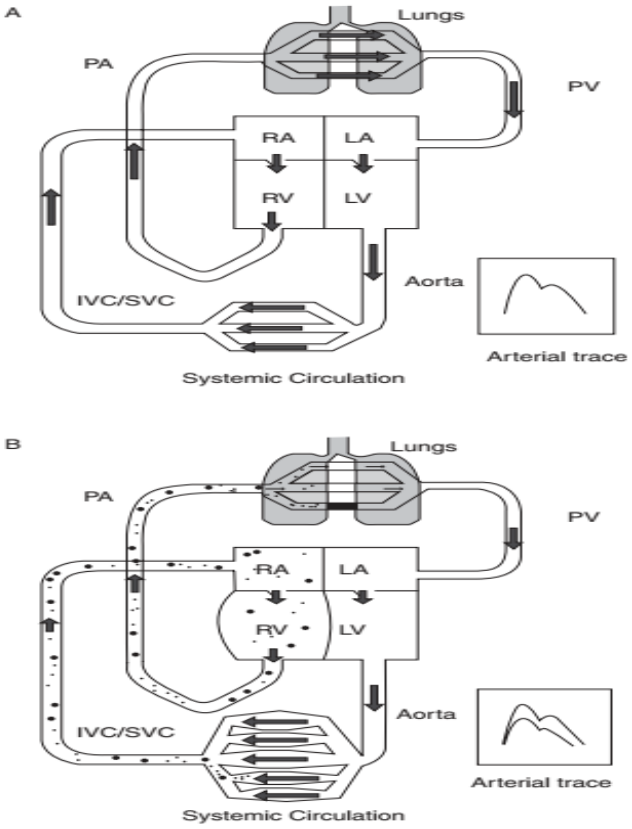

Figure 3. (A) Illustrating Typical Circulation and (B) Presenting a Suggested Integrated Model. This suggested model includes peripheral vasodilation, reduced venous return, increased pulmonary vascular resistance, pulmonary embolism, decreased cardiac output, and lowered systemic vascular resistance.[4,6]

Table 2. Significant Pathological and Surgical Risk Factors Associated with the Onset of BCIS

Osteoporosis
Bony metastasis
Presence of hip fracture (especially pathologic or inter-trochanteric fractures)
Patients with large femoral canals (≥21 mm)
Revision surgery
Surgery on previously un-instrumented femur
Planned use of long-stem prosthesis
Use of excessive cementing pressure

Patients identified as having a higher likelihood of developing BCIS should be assessed to see whether it is possible to use an uncemented fixation method for the prosthesis. Using uncemented prostheses has been shown to efficiently reduce intramedullary pressure in comparison to cemented prostheses. Multiple studies have proven that high-risk individuals get more positive results in relation to pulmonary and cardiovascular problems. Nevertheless, the effect on death rates remains uncertain. Studies have shown that there is an increased risk of death during the period immediately before, during, and after a surgical procedure when bone cement is used. However, this risk decreases significantly after 30 days and becomes

almost nonexistent after 1 year. Previous discussions have addressed the likelihood of early perioperative death in high-risk patients. Two recent investigations have shown that there are no differences in early post-operative mortality or cumulative 1-year mortality between uncemented and cemented hip arthroplasties. Furthermore, evidence from many studies indicates that the use of uncemented hip arthroplasty, especially in instances of hip fractures, is associated with higher levels of discomfort, reduced joint functioning, and an increased need for revision surgeries. Conversely, newly published research discovered no variations connected to the technique used to secure anything in place in terms of pain levels, quality of life, or the risk of death within one year. Currently, there is no standardized and universally acknowledged approach to anaesthesia management aimed at mitigating or addressing the adverse effects of bone cement. A comprehensive assessment and comprehension of the risk factors linked to BCIS, such as bispectral Index-guided depth of anaesthesia and cerebral state index, are crucial. These factors should form the basis for formulating a tailored anaesthesia plan to the individual patient's requirements, overseen by the anaesthesiologist. Table 3 presents the pertinent risk factors relevant to anaesthesia and their contribution to BCIS development. Effective communication between the anaesthesiologist and surgeon is paramount and should take precedence over specific anaesthetic or surgical methodologies.[4,6,18-20,30]

Table 3. Outlines the Anaesthesia-associated Risk Factors Implicated in the Onset of Bone Cement Implantation Syndrome (BCIS) in Individuals Suffering from Femoral Hip Fractures.[4,6,31]

ASA class 3 or 4
Older age
Male gender
Medication with diuretics
Medication with warfarin
COPD
Severe cardiopulmonary disease
Pre-existing pulmonary hypertension

The available evidence concerning the impact of the anaesthesia method on BCIS is limited. General recommendations include maintaining normovolemia perioperatively, preventing anaemia, and administering a high inspired oxygen fraction (FiO_2) to optimize preload, afterload, and oxygen delivery. Advanced haemodynamic monitoring, including continuous cardiac output (CO) measurement, is advised to promptly detect BCIS in high-risk patients, allowing for immediate initiation of supportive therapy and cardiopulmonary resuscitation. Securing the airways and providing high inspired oxygen concentrations should be the top priorities of first therapy, especially for patients with severe cardiopulmonary illness, pre-existing pulmonary hypertension, advanced age, male gender, diuretic or warfarin medication, COPD, or old age. It is essential to rapidly commence cardiovascular support utilizing α- and β-adrenergic sympathomimetic medications. The decision between general and regional anaesthetic, however, doesn't seem to matter all that much. Only a shorter hospital stay was linked to regional anaesthesia, with no differences in mortality, according to a retrospective study involving 56,729 patients that examined mortality rates and length of hospital stay following hip fracture repair by comparing spinal or epidural anaesthesia with general anaesthesia. There were no differences in mortality between regional and general anaesthesia used for hip fracture repair, according to a new Cochrane analysis that included 31 trials. However, investigations on animals have shown that using inhalational anaesthetics might cause haemo dynamic instability. In order to reduce circulatory instability

during cementation during surgery, Khanna et al. advocated avoiding excessive vapour concentrations.[6,20,21,32]

Case Illustration

A 75-year-old woman with a history of osteoporosis and well-controlled hypertension was admitted for a hemiarthroplasty following a displaced femoral neck fracture. Preoperative evaluation revealed normal cardiac function, with an echocardiogram showing a left ventricular ejection fraction of 60% and no signs of right heart dysfunction. Standard intraoperative monitoring, including electrocardiography (ECG), pulse oximetry, and invasive blood pressure measurement, was established.

During the procedure, after insertion of the cemented femoral stem, the patient developed sudden and profound hypotension (blood pressure dropped from 130/80 mmHg to 70/40 mmHg), hypoxaemia (oxygen saturation decreased from 98% to 85%), and tachycardia (heart rate increased to 120 beats per minute). Shortly after, the patient exhibited altered mental status and cyanosis. The surgical team halted the procedure and alerted the anaesthesia team, suspecting BCIS based on the temporal relationship to cementation and the characteristic clinical presentation.

The patient exhibited classic features of BCIS, including sudden hypotension, hypoxaemia, and cardio vascular instability immediately following cement application. The altered mental status suggested cerebral hypoperfusion, while cyanosis indicated systemic hypoxia. A differential diagnosis included fat embolism syndrome, myocardial infarction, and anaphylaxis. However, the rapid onset of symptoms following cementation and the absence of other contributing factors strongly supported the diagnosis of BCIS.[1,6,8-10]

The diagnosis was further supported by intraoperative transoesophageal echocardiography (TEE), which showed right ventricular dilation and reduced contractility, consistent with acute pulmonary hypertension from embolization. Additionally, TEE revealed the presence of echogenic material in the pulmonary arteries, confirming embolic obstruction. Laboratory tests showed elevated lactate levels (indicating tissue hypoperfusion), mild leukocytosis, and no evidence of myocardial injury on cardiac enzymes.

Management focused on stabilizing the patient's haemodynamic and respiratory status. The surgical team minimized further manipulation to prevent additional embolization. The anaesthesiology team initiated aggressive resuscitation with intravenous fluids to improve preload and maintain adequate cardiac output. Vasopressors, including norepinephrine, were administered to counteract systemic hypotension and improve coronary perfusion.[14,25,26]

High-flow oxygen was delivered to address hypoxaemia, and the patient was intubated due to worsening respiratory status and inadequate oxygenation. To reduce pulmonary vascular resistance, inhaled nitric oxide was considered but not immediately required. Continuous monitoring with TEE-guided haemodynamic optimization, ensuring right ventricular function was supported.[6,20,21,32]

The surgical procedure was successfully completed after stabilization, and the patient was transferred to the intensive care unit (ICU) for postoperative monitoring. Over the next 48 hours, the patient's haemodynamics improved, and she was weaned off vasopressors and extubated. This case illustrates the typical presentation of BCIS, with acute cardiovascular and respiratory collapse occurring after cement application. Early recognition, prompt resuscitation, and perioperative vigilance were critical in ensuring a positive outcome. Preventative measures, such as optimizing preoperative status and considering cementless prostheses in high-risk patients, could further reduce the incidence of BCIS in similar cases.

Conclusion

Individuals undergoing cemented hip hemiarthroplasty for femoral neck fractures are at risk of developing Bone Cement Implantation Syndrome (BCIS), a potentially life-threatening complication. Although severe cases are relatively rare, they are associated with significant morbidity and a high mortality rate within the perioperative period and the first 30 days post-surgery. Therefore, thorough pre-operative assessment is essential, with particular attention to high-risk factors such as elevated ASA scores (>2), chronic obstructive pulmonary disease (COPD), and the use of medications like diuretics or anticoagulants (e.g., warfarin). While current strategies focus on risk identification and intraoperative vigilance, the complex, multifactorial nature of BCIS underscores the urgent need for ongoing research. Further studies are vital to deepen our understanding of its pathophysiology, improve risk stratification, and develop more effective preventive

and therapeutic interventions to enhance patient safety and outcomes.

Conflict of Interest

The authors declare no conflicts of interest.

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