# Understanding Bone Cement Implantation Syndrome

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*Bone cement implantation syndrome (BCIS) is a rare and potentially fatal perioperative complication of cemented bone surgery. Clinically, it can be as benign as transient desaturation or mild hypotension. In its more severe presentation, BCIS can cause serious cardiac dysrhythmias and cardiac arrest, and in cemented hemiarthroplasty for femoral neck fracture, BCIS may carry up to a 16-fold increase in 30-day postoperative mortality. The etiology and pathophysiology of BCIS are not fully established; however, results of studies and clinical reports are consistent, citing right ventricular failure secondary to increased pulmonary artery pressure as the cause of systemic hypotension and sudden cardiac arrest. The purpose of this article was to review the literature for a comprehensive understanding of bone cement and BCIS. This article reviews the history of bone cement and its associated hazards, etiology/pathophysiology and clinical presentation of BCIS, preoperative assessment and planning for cemented procedures, anesthetic management of BCIS, and the surgeon's role in reducing the risk of BCIS.*

***Keywords:*** Anesthesia, arthroplasty, bone cement implantation syndrome, methyl methacrylate.

The United States has the highest incidence of total knee arthroplasty in the world, accounting for 9% of inpatient surgical admissions. Currently, more than 1 million total hip and knee replacement procedures are performed annually, and conservative projections anticipate an increase of 143% by the year 2050.[1,2] Rationale for these amazing numbers include aging baby boomers seeking treatment of advanced arthritis in a quest for improved mobility and quality of life.[2]

With this projected increase in cemented orthopedic procedures, it seems inevitable that anesthetists will encounter more patients presenting with bone cement implantation syndrome (BCIS). *Bone cement implantation syndrome* is defined as "hypoxia, hypotension or both, and/or unexpected loss of consciousness occurring around the time of cementation, prosthesis insertion, reduction of the joint, or limb tourniquet deflation in a patient undergoing cemented bone surgery."[3]

• ***Bone Cement: Polymethyl Methacrylate.*** Polymethyl methacrylate (PMMA) is a synthetic resin first developed and marketed under the name Plexiglas in 1928. Due to its biocompatibility, PMMA became an important component of replacement intraocular lenses, dentures, and dental fillings. Sir John Charnley is credited for using it as a prosthetic fixative during a total hip replacement in 1957. By 1965, Sir Charnley's generic PMMA had evolved into bone cement specifically designed for orthopedic procedures.[4]

Bone cement is composed of 2 substances, the "pearls," which are small particles of pre-polymerized PMMA (the white powder), and a liquid monomer of methyl methacrylate (MMA). As the substances are mixed, a catalyst in the liquid initiates the polymerization process. The bone cement hardens as individual pearls are entrapped and sealed in the net of the polymerized monomer.[4,5] Cement is somewhat of a misleading term as it implies some degree of adhesiveness. In the case of bone cement there is no intrinsic adhesive properties. The cement acts as "grout," filling empty spaces and creating tight holds between the implant and irregular bone surfaces.[5]

Numerous additives have been tried in bone cement: antibiotics, radiopaque agents, silver, and vitamin E. Most additives have little or no effect on the quality of the cement or the incidence of BCIS. Antibiotic doses exceeding 2 g have been shown to weaken some of the cement's mechanical properties.[5]

• ***Bone Cement as Occupational Hazard.*** Bone cement poses a potential danger to patients and is a known occupational hazard to persons working with and around cement during mixing and application.[6-8] There are 4 major focuses of concern: vapors, skin, nervous system, and reproductive system.

Every effort should be made to restrict vapor in the air from exceeding 120 to 125 ppm.[7,8] Proper ventilation of the operating room is essential. Vacuum mixing systems not only reduce cement porosity and the potential for air emboli to the patient but also reduce monomer evaporation into the room and exposure to personnel.[5] Vapors may cause irritation to the respiratory tract, eyes, and possibly the liver. Persons wearing contact lenses should not be involved in cement mixing.[8]

Direct contact with liquid can cause itching, burning, redness, swelling, and cracking of the skin. During polymerization, bone cement's exothermic reaction releases heat, which may be damaging to the patient or surgical staff's bone and tissues. Repeated skin contact can cause

dermatitis and allergic reaction. Prolonged skin contact may cause tingling, numbness, and whitening of the fingers. Methyl methacrylate easily penetrates most ordinary clothing and can also penetrate surgical gloves. Should the liquid component come in contact with surgical gloves, the gloves may dissolve and damage to tissue may occur.[8-10] Wearing 2 gloves on each hand and strict adherence to the manufacturer's mixing instructions may diminish skin exposure. The mixed cement should "not make contact with the gloved hand until the cement has acquired the consistency of dough."

Overexposure to MMA can result in central nervous system symptoms. Reported symptoms include headache, drowsiness, nausea, weakness, fatigue, sleepiness, irritability, dizziness, and loss of appetite.[9,10] Minimizing vapors and wearing 2 gloves per hand are again useful ways to limit exposure.

Lastly, high levels of MMA in animal studies have been shown to cause birth defects.[9,10] Therefore, the US Food and Drug Administration (FDA) recommends that pregnant women avoid overexposure because "the safety of bone cement in pregnant women or in children has not been established. Bone cement may adversely affect bone growth and fetal health."[8] Additionally, the FDA cautions that the liquid monomer is highly volatile and flammable. Ignition of monomer fumes by electrocautery devices has occurred in the presence of freshly implanted bone cement.[8]

Should there be a MMA liquid spill, the Association of periOperative Registered Nurses (AORN) 2017 guidelines suggest that the spill area should be isolated, all sources of ignition should be removed, the liquid should be covered with an activated charcoal absorbent, appropriate personal protective equipment should be worn, cleanup should be according to the manufacturer's instructions, the waste should be disposed of in a hazardous waste container, and the spill area should be ventilated until the odor has dissipated.[7]

## Bone Cement Implantation Syndrome

• ***Etiology and Pathophysiology.*** This syndrome is classified according to severity of symptoms (Table 1) generally ranging from grade 1, moderate hypoxia and hypotension, to grade 3, cardiovascular collapse.[4-6] Yet the etiology and pathophysiology of BCIS is not fully established. Early theories focused on circulating MMA monomers; however, recent evidence proposes an embolus-mediated model. Not all documented BCIS phenomena can be explained by the embolus theory alone, and further research is needed in this area.[4,11] Additional proposed theories focus on the role of histamine release, complement activation, and multimodal possibilities. Nearly all the studies and models used to explain BCIS are based on research involving hip arthroplasties.[3,4,11]

• *Monomer-Mediated Model.* Based on the knowledge that circulating MMA monomers could cause vasodilation, early in vivo studies theorized this as the basis for the pulmonary and cardiovascular effects seen in BCIS. However, numerous animal studies disputed this possibility and determined that the plasma MMA concentrations seen in cemented hip arthroplasty were insufficient to cause the cardiopulmonary cascade of BCIS.[3] Subsequent studies have since focused on increased intramedullary pressures at cementation as a causative factor in embolization and BCIS.[4]

| Grade | Clinical criteria |
|---|---|
| Grade 1 | Moderate hypoxia ($Spo_2$ < 94%) or hypotension (fall in SBP > 20%) |
| Grade 2 | Severe hypoxia ($Spo_2$ < 88%) or hypotension (fall in SBP > 40%) or unexpected loss of consciousness |
| Grade 3 | Cardiovascular collapse requiring CPR |

**Table 1.** Grading of Bone Cement Implantation Syndrome[3,6]

Abbreviations: CPR, cardiopulmonary resuscitation; SBP, systolic blood pressure; $Spo_2$, oxygen saturation measured by pulse oximetry.

• *Embolic Model.* Postmortem and echocardiography studies have confirmed the appearance of multiple small emboli in the right atrium, right ventricle, and pulmonary vasculature during surgery. Emboli may be fat, marrow, cement, air, bone, or platelet aggregates in origin.[3,4,11] It is theorized that these multiple emboli have both mechanical and mediator effects.

Emboli are formed because of the high intramedullary pressures (> 300 mm Hg) that occur at cementation and prosthesis insertion. The exothermic reaction of the cement expands the space between prosthesis and bone, thus trapping air and debris, which is forced into the circulation.[3,4] Prosthesis insertion into the cemented femur results in a greater pressure than cementation alone, and if the cement is inserted using a cement gun, rather than manual packing, the pressures generated are almost double.[12] It has been theorized that drilling a vent distal to the prosthesis would allow for pressure escape and would minimize embolization; however, only one study has tried this technique, and it had major equipment flaws associated with pressure measurement.[13]

Several studies used transesophageal echocardiography (TEE) to confirm embolization during cemented hip arthroplasty. Embolic load is greater in cemented vs uncemented hip arthroplasty. Typically, embolization, described as "snow flurries" or "embolic showers," is most pronounced during reaming of both femur and acetabulum, during insertion of prosthesis, and at reduction of the joint (Figure 1).[3,14]

Animal studies have demonstrated the presence of fat and marrow in the pulmonary microvasculature in both cemented and uncemented arthroplasty; however, dogs

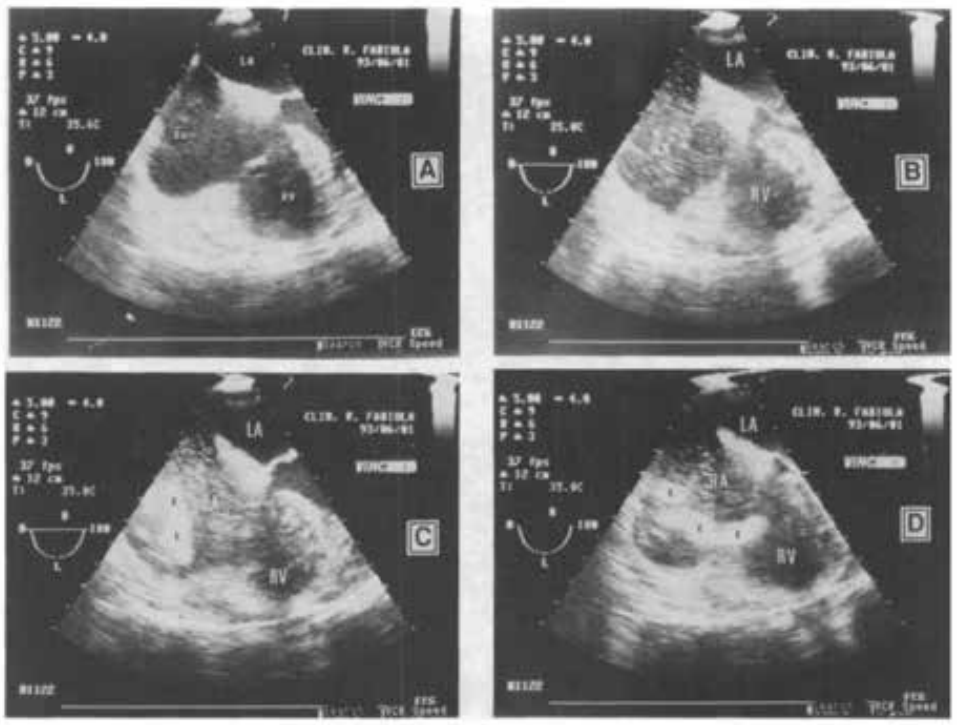


**Figure 1.** Four-chamber transesophageal echocardiographic views showing embolism during total hip arthroplasty: (A) control view, (B) "snow flurry" in the right atrium, (C) small and large emboli in the right atrium, (D) large emboli in the right atrium with delayed passage at tricuspid valve.
Abbreviations: E, embolus; LA, left atrium; RA, right atrium; RV, right ventricle; SF, snow flurry.
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having the cemented procedure had more than a 10-fold increase in the number of emboli.[3] In both procedures the number of emboli was significantly reduced if medullary lavage was performed before cementation and/or prosthesis insertion.[3,4,11] Postmortem examinations following intraoperative deaths during cemented hip arthroplasty confirm pulmonary emboli consisting of fat, bone, and MMA microparticles.[3,4] However, as there is a finite amount of debris present during arthroplasty, there appears to be a "ceiling effect" for the amount of embolization possible irrespective of pressurization.[3]

Hemodynamically, emboli travel to the lungs, heart, and cerebral and coronary circulations. Although the emboli showers may explain the hypoxia, right ventricular (RV) dysfunction, and hypotension of BCIS, research has not established a link between cardiovascular compromise and embolic load.[3]

Emboli-released mediators may result in increased pulmonary vascular resistance (PVR; Figure 2). Bone cement emboli may mechanically stimulate or cause endothelial damage that generates a reflex vasoconstriction through the release of endothelial mediators. Embolic substances also directly increase PVR by raising blood levels of thrombin and tissue thromboplastin. Other mediators, 6-keto prostaglandin F1α and tissue thromboplastin can also cause a reduction in systemic vascular resistance (SVR) by releasing secondary mediators such as adenine nucleotides or by acting indirectly to promote release of mediators such as platelet-derived growth factor, serotonin, thromboxane A2, platelet activating factor, and adenosine diphosphate. Serotonin is the most pronounced mediator released.[3,15] It is a powerful pulmonary vasoconstrictor, yet it causes dilation of peripheral arterioles. Together, the increased PVR in the presence of decreased RV preload results in a marked decrease in cardiac output (CO). As the CO becomes increasingly affected, hypotension worsens.[15] Medullary lavage before cementation and/or prosthetic insertion can reduce the release of some mediators. Clinically, it is the increase in PVR and ventilation perfusion mismatch that manifests as patient hypoxemia.[3]

Although the embolic model is the dominant hypothesis, it has some problems. First, embolization is not always associated with hemodynamic changes, nor does the degree of embolization correlate with the severity of cardiopulmonary effects in patients.[3] Results of TEE have shown that although embolic events are frequently observable, most patients tolerate them well. This has led current researchers to believe that microembolism may be a contributing factor, rather than the primary mechanism of BCIS.[3,4,14]

• *Histamine Release and Hypersensitivity*. Anaphylaxis

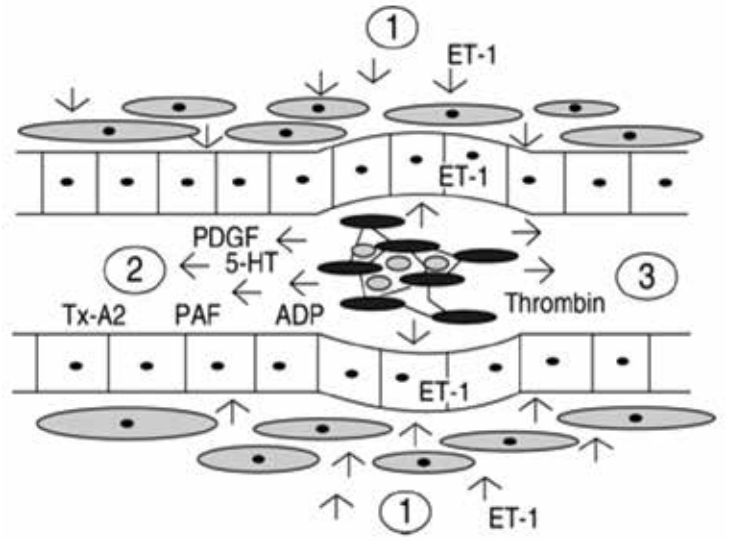


**Figure 2.** Pulmonary vessel with embolus comprising fat, platelets, fibrin, and marrow debris. (1) Reflex vasoconstriction and endothelial production of endothelin 1 (ET-1). (2) Release of vasoconstriction mediators; platelet-derived growth factor (PDGF), serotonin (5-HT), thromboxane $A_2$ (Tx-A2), platelet activating factor (PAF), adenosine diphosphate (ADP). (3) Vasoconstriction attributable to noncellular components of embolus, including thrombin.
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and BCIS have numerous clinical similarities. Increased plasma histamine concentrations have been documented in hypotensive patients undergoing cemented hip arthroplasty. There are no studies confirming the cause of the histamine release, whether it is a direct effect of MMA or through an IgE-mediated process. One study did find that blockade of histamine receptors, using clemastine and cimetidine ($H_1$ and $H_2$ antagonists), did provide some protective effect; however, 2 subsequent studies were unable to replicate those findings.[6,15]

• *Complement Activation.* Anaphylatoxins C3a and C5a are potent mediators of vasoconstriction and bronchoconstriction. Under normal conditions, they complement the immune response and our natural defenses. In cases of BCIS, via either hypersensitivity reaction or a direct effect of the cement, the increased levels of C3a and C5a result in smooth muscle contraction, histamine release, and increased vascular permeability. This manifests clinically as pulmonary vasoconstriction, desaturation, and systemic hypotension (Figure 3).[3,4] Increased C3A and C5a levels have been demonstrated in cemented vs uncemented hip arthroplasty, suggesting activation of a complement pathway.

• *Multimodal Model.* A combination of the theorized models in conjunctions with individual physiologic response is the most likely explanation for BCIS. Preexisting comorbidities, surgical technique, and proposed surgery itself may also alter a patient's response to bone cement.[3]

• ***Anesthetic Literature Review.*** Hemiarthroplasty is an often-performed surgical procedure,[2] and most documented case studies involving BCIS have occurred during cemented hip hemiarthroplasty.[16] In 2009 the National Patient Safety Agency (NPSA) of the United Kingdom (UK) issued an alert concerning the use of cement during hip arthroplasty,[17] which prompted several large-scale observational studies to determine best anesthetic practice for hip arthroplasty.

In 2014, White et al[18] published a large observational study of 65,535 patients undergoing hip fracture surgery. Looking at mortality rates, these researchers collected data from the UK's National Hip Fracture Database for the year 2012. The researchers investigated mortality rates with 3 data collection points: within the first 24 hours, within 5 days, and within 30 days.[18] Comparing mortality rates for patients undergoing general anesthesia (30,130 patients) vs spinal anesthesia (22,999 patients), they found no significant difference in anesthetic technique and mortality rate at either the 24-hour mark or within 5 days. Likewise, once adjustments were made for age and ASA classification, there was no significant difference in 30-day mortality rates for general anesthesia vs spinal anesthesia. However, it is important to note that within 24 hours of surgery, mortality was significantly higher in cemented hemiarthroplasty compared with uncemented, suggesting that BCIS may play a role in perioperative mortality.[18]

The 2004 Cochrane Database Review of hip fracture surgery[19] recommended spinal anesthesia over general anesthesia. This review article became the basis for subsequent guidelines in the UK.[18] However, in 2015,

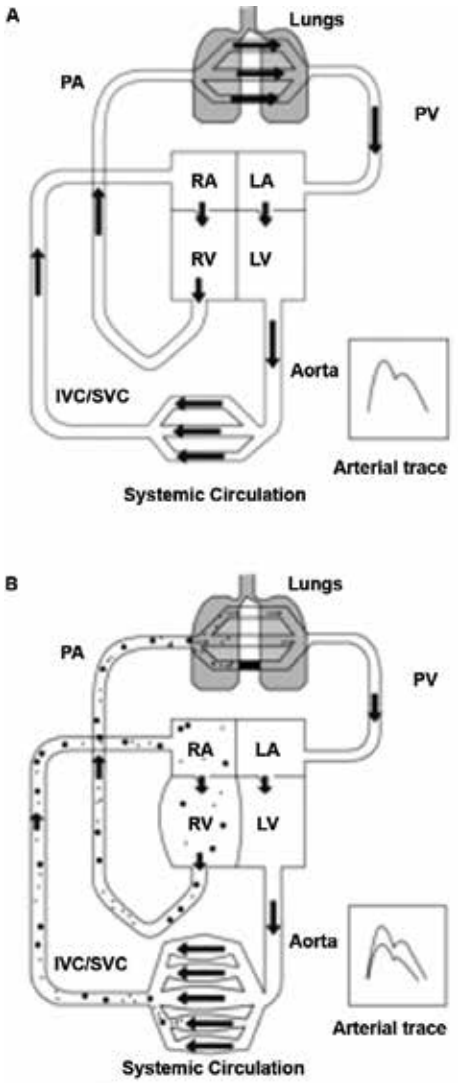


**Figure 3.** A. Normal circulation. B. Proposed combined model with peripheral vasodilation, reduced venous return, increased pulmonary vascular resistance and pulmonary embolization, reduced cardiac output, reduced systemic vascular resistance (allowing some counterincrease in cardiac output due to reduced afterload) and hypoxia from both the emboli and the pulmonary effects of histamine.

Abbreviations: LA, left artery; LV, left ventricle; PA, pulmonary artery; RA, right artery; RV, right ventricle.

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Parker and Griffiths[20] conducted a pilot study of 322 patients and found no differences in mortality, blood transfusions, and postoperative complications between general and spinal anesthesia. Furthermore, an updated Cochrane Database Review in 2016 found no differences in general and spinal anesthesia when the researchers compared data from 3,231 participants in the areas of mortality, pneumonia, myocardial infarction, cerebrovascular accident, acute confusional state, or patient return to their own home.[21]

Neumann et al[22] conducted a retrospective study in New York and collected data from 18,158 patients at 126 hospitals. Unadjusted in-hospital mortality was equivalent between anesthetic techniques. Only after applying a 21-variable case mix adjustment to the data did the researchers conclude spinal anesthesia to be associated with a lower in-hospital mortality rate.[22]

The inability of these very large observational review studies to detect significant differences in patient mortality suggests a need for randomized controlled studies concerning best practices for hip arthroplasty. Furthermore, the need for multiple variable adjustments suggests the definitions of general anesthesia and spinal anesthesia may be too broad for practical clinical recommendations. Perhaps future studies about best anesthetic practice should explore the *best method* for general anesthesia or the *best method* for spinal anesthesia.[18]

A retrospective study published in 2016 evaluated the incidence of BCIS in spinal-epidural anesthesia vs single epidural anesthesia for hemiarthroplasty.[16] The medical records of 1,210 patients over a 5-year timeframe were reviewed. Numerous patient high-risk identifiers were included in the study; however, patients with preexisting arrhythmias, dementia, and chronic obstructive pulmonary disease (COPD) were excluded. Overall, 72.2% of all patients demonstrated some degree of BCIS (grade 1 or greater). Furthermore, the researchers claimed the spinal-epidural anesthetic to be a better choice over epidural alone.[16] However, because it is a retrospective study, there are definite gaps in the provided information. Anesthetic technique is identified solely as "spinal-epidural" or "epidural only," and there is no mention of agent, dose, or concentration of local anesthetic. No information is given concerning level of sedation, level of blockade, or adjunct anesthetic agents. Also concerning is a disclosed limitation concerning the quality of the medical records themselves.

If best anesthetic practice for hip arthroplasty has yet to be identified, it stands to reason that best practices to prevent the potential, but rare, adverse effects of BCIS have yet to be defined. However, careful preoperative assessment of the patient and identification of individual patient risk factors should guide the anesthetist to develop an anesthetic plan that maximizes each individual's cardiopulmonary health. Indeed, safety guidelines for cemented hemiarthroplasty published in 2015 stress identification of high-risk individuals, vigilance during cementation, aggressive resuscitation in the event of BCIS, and good communication between surgeon and anesthetist, rather than naming a specific technique.[23]

Cardiopulmonary changes and embolism have also been reported in low-injection-pressure procedures such

as percutaneous vertebroplasty and kyphoplasty.[24,25] Cement leakage is one of the more common complications of vertebroplasty and has been associated with hemodynamic changes and embolism of cement into the vasculature.[24-26] In 2016, Zhu et al[26] used postoperative x-ray images to measure the incidence of bone cement leakage during percutaneous vertebroplasty and determined the 2 strongest risk factors for cement leakage to be the severity of the fracture itself and the volume of cement used. An advantage of balloon kyphoplasty over percutaneous vertebroplasty is the ability to inject the bone cement at a lower pressure. Kyphoplasty allows for the insertion of a very viscous cement to be injected slowly at a much lower pressure. Reducing injection pressure results in a corresponding reduction in cement leakage, with the incidence of leakage being 19.7% for vertebroplasty and 7% for kyphoplasty.[24] In the event of multilevel kyphoplasty, staged balloon inflation vs simultaneous inflation also reduced the incidence of cardiopulmonary complications associated with cement leakage.[24]

Bone cement implantation syndrome presents a challenge for anesthetists. There is consistent documentation of intraoperative cardiopulmonary compromise that correlates to specific points in the surgical procedure. However, there continues to be a lack of confidence in the literature as to the best anesthetic technique for cemented bone surgery.[3,4,11] Therefore, preoperative evaluation and constant intraoperative vigilance remain key in the prevention and management of BCIS.

• ***Preoperative Assessment and Planning.*** Prevention of BCIS begins with identifying high-risk patients during the preoperative assessment (Table 2). Communication between surgical, anesthetic, and medical providers is essential for high-risk patients with numerous or severe risk factors or comorbidities.[23] Older adults aged 65 years or greater are more likely to experience some degree of BCIS, and patients aged more than 85 years experience significantly more hemodynamic changes during cemented bipolar hip arthroplasty.[27] Preoperative preparation of older adults should, therefore, be aimed at maximizing cardiopulmonary stability and any preexisting comorbidities before surgery. Invasive hemodynamic monitoring may be needed for the management of this population.

Severe cardiopulmonary disease, preexisting pulmonary hypertension, and porous bone quality (osteoporosis) are risk factors for BCIS.[4,11,28] Chronic obstructive pulmonary disease is an additional risk factor, as it is often complicated by pulmonary hypertension and increased PVR. Underlying COPD, in the event of BCIS, has an additive effect to hypoxia, acidemia, and the overall inflammatory response.[6] High oxygen concentrations should be considered, especially at high-risk times (reaming, cementing, reduction of joint, and deflation of tourniquet).[4] A rapid unexplained drop in end-tidal carbon dioxide ($ETCO_2$) is an early indicator of BCIS,

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|---|
| ASA class 3 or 4 |
| Older adult |
| Male sex |
| Use of diuretics |
| Use of warfarin |
| Chronic obstructive pulmonary disease |
| Severe cardiopulmonary disease |
| Preexisting pulmonary hypertension |
| Osteoporosis |
| Bony metastasis |
| Presence of hip fracture (especially pathologic or intertrochanteric fractures) |
| Patients with large femoral canals (≥ 21 mm) |
| Revision surgery |
| Surgery in uninstrumented femur |
| Planned use of long-stem prosthesis |
| Use of excessive cementing pressure |

**Table 2.** Risk Factors Associated With Bone Cement Implantation Syndrome[3,4,6]

capnography is indicated whether the patient undergoes general or regional anesthesia. Hypoxia is also a cardinal sign of BCIS, making pulse oximetry essential.[29]

Early hemodynamic indicators of BCIS are bradycardia and hypotension. Continuous electrocardiography (ECG) and maintenance of systolic blood pressure to within 20% of baseline is ideal.[27] Invasive arterial blood pressure monitoring may be indicated in the face of hemodynamic instability, an anticipated need for frequent arterial blood gas analysis, anticipated use of vasopressors, or a patient with multiple BCIS risk factors.[29] Inhalational agents have been reported to cause more profound hemodynamic effects in the presence of BCIS, and nitrous oxide should be avoided in patients with BCIS to prevent exacerbation of air embolism.[3,4,11]

Intravascular fluid volume should be kept as close to normal as possible. Anemia is common among adults over age 65 years (17%), and in the hip fracture population the incidence of anemia is even greater (50%). Preoperative and intraoperative blood and fluid resuscitation of the patient should be considered.[30] Central venous pressure monitoring may aid volume optimization; however, should the patient experience BCIS and increased pulmonary artery pressures, the central venous pressure may become ineffective. Intraoperative cardiac output monitoring may be indicated in patients with 1 or more risk factors.[4] Cardiac output monitoring can take the form of semi-invasive transesophageal Doppler monitoring or invasive cardiac output monitors such as a pulmonary artery flotation catheter.[4]

Regional anesthesia with little or no sedation allows for evaluation of mental status and dyspnea during ar-

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|---|
| Hypoxia |
| Hypotension |
| Unexplained loss of consciousness |
| Pulmonary hypertension |
| Pulmonary edema |
| Bronchospasm |
| Cardiac dysrhythmia |
| Hypothermia |
| Thrombocytopenia |
| Cardiac arrest |

**Table 3.** Clinical Signs of Bone Cement Implantation Syndrome[3,4]

throplasty.[27,29] However, this should be weighed against the need for a secure airway and maximum ventilation in the event of BCIS.

All information obtained during assessment should be communicated among the operative team and used to optimize patient outcomes. Although BCIS usually presents intraoperatively, there has been a case report of delayed BCIS presentation.[11] Postanesthesia care unit (PACU) personnel should be aware that hypoxia, hypotension, unexplained loss of consciousness, anaphylactic reactions, or pulmonary hypertension may be manifestations of BCIS and should be promptly treated.[31]

• ***Clinical Presentation.*** Clinically, BCIS can be as benign as transient desaturation or mild hypotension, or as serious as cardiac dysrhythmias and arrest. Typically, it manifests at the time of cementation, prosthesis insertion, reduction of joint, or deflation of tourniquet.[3,4,11] However, there is one documented case report of a delayed presentation that occurred in the PACU.[11] Table 1 shows how the severity of BCIS has been classified into 3 grades based on severity of clinical presentation.[3] Being able to grade the severity of patient responses has identified perioperative mortality rates (died within 48 hours of surgery) for grade 2 and grade 3 BCIS as 2% and 95%, respectively.[6]

Studies and clinical reports are consistent, citing RV failure secondary to increased pulmonary artery pressure (PAP) as the cause of systemic hypotension and sudden cardiac arrest.[3,4,6,11] Whether the causative factor is mechanical or mediated, during BCIS the RV rapidly dilates and shifts the interventricular septum to the left. This shift decreases the functional size of the left ventricle (LV), as the total volume (size) of the heart cannot expand within such a rapid timeframe because of the physical constraints of the pericardium.[4] These acute cardiovascular changes cause an immediate decrease in LV compliance, reduced ventricular filling, and reduced cardiac output. Increased RV pressure and decreased cardiac output may lead to decreased coronary perfusion pressure and cardiac ischemia.[11] Emboli in the cerebral circulation have also been detected via transcranial Doppler imaging. The presence of these cerebral emboli has been cited as a possible explanation for the postoperative delirium seen in older adults undergoing cemented hip arthroplasty.[32] Clinical signs of BCIS (Table 3) plus the sudden reduction in $ETCO_2$ are strong indicators of BCIS; however, a definitive diagnosis is made by computed tomographic scan.[11]

• *Management.* Early detection of BCIS is crucial for patient survival. Rapid initiation of aggressive supportive therapy is key to optimizing patient outcomes.[3,4,28,33] If BCIS is suspected, initial treatment includes securing the airway, increasing inspired oxygen concentrations ($FIO_2$) to 100%, and accurately monitoring $ETCO_2$.[4,27,29,33] Cardiopulmonary resuscitation should be initiated if needed. If one is using a propofol infusion, decrease or discontinue its use until the patient is hemodynamically stable.[15] Pulmonary vasodilators (inhaled nitric oxide or prostaglandin E1) may be needed to decrease the PAP should hypoxemia and RV dysfunction worsen.[4]

Invasive monitoring may be needed. Central venous pressure lines help guide and administer fluid therapy, although central venous pressure may not be reliable in high PAP states. Fluid therapy should be aimed at maintaining normovolemia.[4] Fluid resuscitation with blood or blood products should be considered because the reduced ability of the circulation to deliver oxygen to vital organs may be exacerbated by a preexisting anemia.[30]

Cardiovascular collapse should be treated as RV failure. Direct-acting α-1 agonists (epinephrine, norepinephrine) may be needed to maintain hemodynamic stability.[3,27,29,33] Ephedrine, an α- and β-adrenergic agonist, may be given in cases of bradycardia and hypotension, but one should be alert giving any sympathomimetics without addressing pulmonary vasoconstriction, because this may result in rapidly increased RV preload and acute RV failure.[15] Inotropes, such as dobutamine and milrinone, may be given to maintain RV contractility.[4,29,33] Glycopyrrolate, an anticholinergic, may be given as a preemptive or rescue medication to counteract possible intracardiac chemoreceptor mediated vasovagal reaction.[15]

Cardiac output monitoring via TEE or pulmonary artery floatation catheter to guide fluid, vasopressor, and inotrope therapies may be indicated.[4,11]

Sodium bicarbonate may be given to correct metabolic acidosis.[29] Corticosteroids have been used to counter any inflammatory or anaphylactoid reactions of BCIS but should also be considered preoperatively with any preexisting hyperallergic, mast-cell activation, or inflammatory comorbidities.[29,34]

Ondansetron, a 5-hydroxytryptamine3 (5-HT3) receptor antagonist, has been given preoperatively and intraoperatively to block serotonin-induced pulmonary vasoconstriction.[15] Likewise, histamine-receptor blockade with $H_1$ and/or $H_2$ antagonists (clemastine and cimetidine) has also been used preoperatively and intraoperatively

to block the direct effects of cement on histamine release or to block the IgE-mediated process of hypersensitivity (anaphylaxis).[3]

Although pulmonary artery pressures usually normalize within 24 hours, patients should be monitored in the intensive care unit postoperatively.[3,4,11] Patients with no preexisting heart disease usually recover rapidly. However, in 2014, during hip arthroplasty, an incidence rate of 1 death or severe harm per 2,900 cases was reported in the UK, and the BCIS cascade was described as an acute deterioration, with 80% of associated patient deaths occurring on the operating room table.[35]

• ***Surgery's Role.*** Understanding surgical rationale for techniques and choices is essential to good communication among the operating room team members. There are several surgical measures that can be taken to reduce the risk of BCIS. Cement-less prosthesis would seem like a likely choice to avoid BCIS. However, when investigators compared noncemented with cemented arthroplasty for hip fractures, cemented arthroplasty led to less residual pain, better mobility, and reduced need for revisions.[36] Perioperative mortality has been shown to be significantly higher in cemented hip hemiarthroplasty compared with uncemented technique. However, at the 1-year mark, mortality rates reversed, with a more favorable survival for patients with cemented hip arthroplasty.[37,38]

If cement is necessary, use of a low-viscosity cement, a short-stem prosthesis, lavaging the intramedullary canal prior to insertion of prosthesis, and obtaining hemostasis before implanting the prosthetic joint can reduce the patient's risk of BCIS.[4,11]

Using a bone-vacuum cementing technique when mixing the cement reduces micropores and macropores in the cement. Decreasing the porosity of the cement, reduces the embolic load of both mechanical and mediator-driven particles. Mixing under vacuum also increases the strength of the cement, delivers consistent cement results, decreases the risk of loosening or cracking of cement, and limits personnel's exposure to cement fumes.[31,39]

Lastly, retrograde insertion of bone cement (distal to proximal), through the use of a cement gun, helps to compartmentalize bone marrow contents. Thus, providing a uniform lower intramedullary pressure and minimizing risk of BCIS.[4,11]

## Conclusion

Occurring in 20% of all femoral fracture repairs,[6] BCIS is a reported complication of any cemented bone surgery. Numerous theories have been proposed to explain BCIS, with more recent researchers considering a multimodal explanation. Clinical presentation is usually hypoxia, hypotension, and an unexpected loss of consciousness occurring at cementation, prosthesis insertion, reduction of the joint, or tourniquet deflation[3] with grades 2 and 3 BCIS resulting in right ventricular failure secondary to increased pulmonary artery pressure.[3,4,6,11] Suspected BCIS should be treated with aggressive resuscitation and supportive care.[4,11] Prevention of BCIS includes identification of high-risk patients, preoperatively optimizing patient risk factors and comorbidities, and good communication with the surgical team.[11,28] Given the projected rise in total joint replacement[1,2] and as anesthesia techniques for joint surgery evolve, evidence-based research is needed to determine best guidelines for anesthetic management of cemented orthopedic surgeries and the rare but potentially deadly complication of BCIS.

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## DISCLOSURES

The author has declared no financial relationships with any commercial entity related to the content of this article. The author did not discuss off-label use within the article.