Bone Cement Implantation Syndrome

PA-PSRS has received reports of six intraoperative cardiac arrests in patients—five resulting in death—associated with hip arthroplasties using bone cement to implant prostheses. While hip surgery is a common procedure among the elderly and generally considered safe and effective, mortality most often occurs postoperatively, usually from cardiopulmonary causes such as myocardial infarction or pulmonary emboli.1

Intraoperative deaths during hip arthroplasty occur less frequently but are almost exclusively associated with cementing of the femoral prosthesis.1,2 Although cardiac arrest and death are the most catastrophic symptoms associated with cemented arthroplasty, bone cement implantation syndrome (BCIS) is a well-recognized complex of sudden physiologic changes that occur within minutes of the use of methyl methacrylate cement to secure a prosthetic component into the femur.1-4 The cardiopulmonary complications of BCIS can be reduced through modern cementing techniques, appropriate anesthesia interventions, and adequate patient preparation, as well as avoiding the use of cement altogether.

This article presents the traditional and current opinions about the theories and causes of BCIS. In addition, this article includes information from the clinical literature on risk factors, risk reduction strategies and treatment.

BCIS: Past and Present
Intraoperative cardiorespiratory changes during total hip arthroplasties have been reported since cemented components were introduced in 1961.5,6 Theories about the cause of BCIS include the following:

- Direct effect of exothermic reaction of cement temperature7-9
- Air or gas embolism caused by polymerization of methyl methacrylate monomer7,8,10
- Hypersensitivity/anaphylactic reaction to the acrylic monomer7,9
- Reflex bradycardia7
- Increase in intramedullary pressure resulting from the introduction of hot acrylic cement (This increase could force marrow and fat into the circulation, producing pulmonary emboli.)7-9

Fat and debris from the femoral shaft embolize from the femoral canal during cement and implant insertion3

Toxic effects of the monomer (These effects may enhance the depressant cardiovascular effect of volatile halogenated anesthetic agents.)7

Toxic cardiovascular effects of methyl methacrylate monomer or additives (These substances may produce hypotension when absorbed into the circulatory system.)5-9

Increased amount of monomer absorbed by the large and well vascularized femoral shaft7-9

Small amounts of toxic, unreacted methyl methacrylate monomer absorbed rapidly into the circulation9,11

Embolic showers that occur during cement pressurization (Experimental studies using transeophageal echocardiography [TEE] indicate that these showers are directly correlated with changes in pulmonary parameters.)5

At one time, methyl methacrylate toxicity was considered the major cause of hemodynamic instability during arthroplasty surgery.5,11 However, this hypothesis has not been confirmed by animal studies. More than 30 times the level of methyl methacrylate ordinarily used in human arthroplasty must be used to produce significant changes in cardiopulmonary parameters.5,11,12 While absorbed monomer temporarily lowers blood pressure after insertion of bone cement, there is little evidence indicating that...
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monomer causes severe systemic reactions.\textsuperscript{13} No correlation has been found between blood pressure changes and monomer concentration.\textsuperscript{5} Moreover, using a dog model, Orsini et al.\textsuperscript{5,11} determined that similar cardiopulmonary changes occur when using either bone cement or inert bone wax, producing high intramedullary pressures that force bone marrow into the circulation at the time of cement and prosthesis insertion.\textsuperscript{5,11} Methyl methacrylate monomer is no longer considered the cause of cardiopulmonary dysfunction during procedures using cemented components.\textsuperscript{5}

BCIS is now considered to be caused by the hemodynamic effects of medullary fat embolism, rather than the toxic effects of the cement itself.\textsuperscript{2,14} Cementing prior to prosthesis insertion causes sealing and pressurization of the femoral canal when the prosthesis is inserted. This leads to high intramedullary pressure, forcing medullary fat into the vasculature. This embolic load produces acute pulmonary hypertension that can lead to right ventricular dysfunction, ischemia, hypotension, and even sudden death.\textsuperscript{1,11,14-16} The severity of these symptoms does not correlate with the amount of methyl methacrylate used.\textsuperscript{16} Moreover, this syndrome occurs in the absence of methyl methacrylate use.\textsuperscript{16} Non-cemented arthroplasty produces lower intramedullary pressures, fewer emboli, and much less hemodynamic disturbance.\textsuperscript{2} TEE has shown that embolization of fat and marrow contents occurs with the insertion of both cemented and uncemented implants.\textsuperscript{1,12} However, the emboli associated with cement are of greater number, size, and duration.\textsuperscript{1}

Trends in Prosthesis Fixation

While fixation of femoral prostheses with cement remains popular, cementless stem fixation has become more durable and clinically effective over the past two decades.\textsuperscript{17} A review of 10,299 primary total hip arthroplasties in the North American Hip and Knee Registry revealed that cement use for stem fixation declined from 66.2% of the procedures in 1995 to 38.6% in 2001 ($p <0.001$). Patients with good bone quality are considered good candidates for uncemented implants, particularly those with thick cortices and small medullary canals.\textsuperscript{18}

Symptoms

An elderly female presented via ambulance following a fall at home. She was diagnosed as having a fracture of the left femoral neck. The patient was medically cleared for surgery based upon physical examination, normal lab work, and a normal electrocardiogram. An urgent left hemiarthroplasty was performed under spinal anesthesia. Intraoperatively, after cementing of the prosthesis, the patient developed hypotension, bradycardia, and cardiac arrest. The surgical field was covered, and the patient was placed in supine position for cardiopulmonary resuscitation. The patient did not respond to resuscitative measures, and she expired.

The preceding account from a report submitted to PA-PSRS is an example of the onset of some BCIS symptoms in a patient. A more complete list of characteristics of BCIS includes the following:

- Systemic, life-threatening hypotension\textsuperscript{2,4,5,14,19,20}
- Pulmonary hypertension\textsuperscript{2,11,14,19,20}
- Increased central venous pressure\textsuperscript{20}
- Pulmonary edema\textsuperscript{11}
- Bronchoconstriction\textsuperscript{11}
- Anoxia/hypoxemia\textsuperscript{1,5,11,14,19,20}
- $P_{ET}CO_2$ decrease\textsuperscript{4}
- Cardiac dysrhythmia/arrhythmias\textsuperscript{1,4,11}
- Cardiogenic shock\textsuperscript{1}
- Cardiac arrest\textsuperscript{1,4,5,11,20}

Figure 1. Diseased Right Hip and Total Arthroplasty Left Hip with Acetabular and Femoral Prostheses
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- Sudden death\(^4,5,20\)
- Fat/marrow emboli\(^2,11,20\)
- Hypothermia\(^11\)
- Thrombocytopenia\(^11\)

Incidence

For patients undergoing total hip arthroplasty with cemented implants, cardiopulmonary changes have contributed to intraoperative mortality ranging from 0.02% to 6.6% of the cases.\(^5,21\) Parvizi et al.\(^1\) reviewed 38,488 hip arthroplasties in 29,431 patients in an institution’s registry and found that the incidence of sudden intraoperative death during any kind of arthroplasty was 0.06%. For patients undergoing arthroplasty as a result of a fracture, however, intraoperative mortality increased to 0.18%. Those with fractures who received cemented arthroplasties had intraoperative mortality rates as high as 0.2% to 4.3%.\(^1\)

Studies using TEE during hip arthroplasty indicate that intracranial and pulmonary emboli occur in from 0.5% to 2% of patients. Moreover, TEE revealed that emboli occur in most patients undergoing femoral medullary reaming and hip hemiarthroplasty.\(^22\) This suggests that embolic events during hip arthroplasty (even subclinical occurrence) are more common than generally recognized.\(^22\)

Pathophysiology

Clinical and laboratory studies of cement implantation syndrome indicate the underlying cause of the systemic hypotension and sudden cardiac failure is right ventricular failure secondary to increased pulmonary artery pressure (PAP).\(^6\) Serious embolization increases the PAP and pulmonary vascular resistance (PVR), causing the thin-walled right ventricle to dilate so that the intraventricular septum shifts to the left.\(^12\) These changes decrease left ventricular compliance, reducing left ventricular filling and cardiac output.\(^23\) The resulting hypotension decreases coronary perfusion pressure. As right ventricular end-diastolic pressure increases, right coronary flow decreases, producing low systemic blood pressure and creating ischemia to the right ventricle.\(^2,23\) This process produces a vicious cycle of right ventricular depression, failure, and death.\(^23\) Such changes can occur within minutes of inserting a cemented prosthesis.\(^2\) Overall, there is a markedly decreased stroke volume of the heart accompanied by increased right ventricular area and decreased left ventricular area.\(^12\)

Embolization is enhanced when tissue thromboplastin from the bone marrow, forced into the veins of the proximal femur during prosthetic insertion, activates a clotting cascade, lesions of the venous endothelium, and thrombogenesis.\(^24\)

Risk Factors

Patient Factors

Elderly patients with underlying cardiovascular disease who are undergoing cemented arthroplasty for repair of a fracture are at greatest risk for developing BCIS.\(^1\) Advanced age has been associated with a higher mortality rate.\(^1,11,25\) Severe osteoporosis may place a patient at higher risk also because osteoporotic bones have enlarged porous cavities and vascular spaces, which may allow marrow contents to enter the venous system more easily.\(^1,11\) Intertrochanteric or pathologic fractures are a risk factor.\(^1,12\) This may be due to the many co-morbid conditions associated with fractures that may increase mortality risk, compared to those patients undergoing elective hip replacement. Moreover, medical optimization may not occur in many fracture cases because of the urgency of surgical repair, increasing the potential for intraoperative mortality. Those with fractures have greater blood loss preoperatively and intraoperatively, contributing to hypovolemia and hypotension.\(^1\) Pathologic fractures may be a risk factor because of pressurization of abnormal vessels in cancellous bone.\(^2\)

Severe underlying cardiovascular disease makes some patients unable to tolerate the pathophysiologic effects associated with the cementing and embolic process.\(^1,11,24\) Patients are susceptible to cardiac ischemia if their preoperative cardiopulmonary reserve is limited by pre-existing pulmonary hypertension, right ventricular dysfunction, or coronary artery disease.\(^2,23,24\)

The pulmonary shunt values of healthy patients or those with mild systemic disease (ASA Class 1 or 2) who sustain embolic events can be re-established uneventfully at the end of the procedure. But, in those with severe systemic disease (ASA Class 3 or 4), pulmonary shunt values are likely to remain abnormally high even postoperatively, increasing the risk of morbidity.\(^24\) The severity of the patient’s pulmonary hypertension in response to embolization is associated not only with the extent of embolization and pre-existing cardiovascular status, but also with the compliance of the pulmonary vasculature and activity of humoral reflex mechanisms.\(^11,12\)

Patients with fixed heart rates cannot compensate when stroke volume decreases.\(^12\) Therefore,
patients with pacemakers or those receiving a sympathetic blockade caused by epidural anesthesia are at increased risk for this syndrome.12

Patients who are hypotensive or who have inadequate volume replacement pre- or intraoperatively are less able to tolerate further ischemic changes associated with this syndrome.

Femoral tumors or cancer place a patient at risk because of potential alterations in the femoral vascular architecture that may increase the risk of marrow embolization.11

Patients with large femoral canals (21 mm or more) are at risk for hypotension when cement is inserted into the femoral canal because of an increased vascular surface and a greater amount of embolizable intramedullary contents.25 Males are more likely to have larger femoral canals than women.25

Severe outcomes from emboli may be more likely in those with a patent foramen ovale (25% of the population), which allows emboli to pass to the right heart (bypassing the lungs) and into the arterial system to the brain.19

Patients who are hemodynamically unstable at the time of cementing and prosthesis insertion are more likely to develop this syndrome.2

The risks of intraoperative death during cemented hip arthroplasty are well known.19-21 In the study by Parvizi et al.1 mentioned previously, involving a review of over 38,000 total joint arthroplasties, 23 intraoperative deaths occurred, all during cemented hip arthroplasty procedures (p<0.001). The cardiovascular collapse of all but three of these patients occurred during the process of cementing. However, in one year, no intraoperative deaths occurred in more than 12,500 patients who had a non-cemented procedure.

The same pattern was evident in a survey of trauma centers in Wales. In one year, 15 intraoperative deaths during hemiarthroplasty occurred in 847 patients having a cemented prosthesis. In the same year, no intraoperative deaths occurred in 328 patients having non-cemented prostheses.20

The major factor in emboli development is increased intramedullary pressure from mechanical compression in the femoral canal, which in turn is produced by the bone cement and insertion of the prosthesis stem.24 The process of cementing produces a transient but significant decline in cardiac output and reduction in stroke volume.25

In a 72-patient prospective randomized clinical trial, the controls received bone cement mixed conventionally, while the experimental group received bone cement mixed in a vacuum. All patients received hemodynamic and transesophageal echocardiography during cemented hip arthroplasty procedures. The incidence of severe cardiac complications and death was significantly reduced in those receiving bone cement mixed in a vacuum.10

**Risk Reduction Strategies**

Surgeons and anesthesiologists can provide major patient safety interventions to reduce the risk of BCIS, including the following:

**Patient Assessment**

- During preoperative and preanesthetic assessments, identify risk factors, particularly the patient’s cardiopulmonary reserve, and use this information to choose the prosthesis, surgical procedure, and techniques most likely to avoid cardiopulmonary complications.1,2,23,27
- If medically feasible, defer surgery until the patient’s medical and cardiovascular status can be maximized.1

**Anesthetic Techniques**

- Maintaining normovolemia,23 particularly at the time of cementing and prosthesis insertion.1,2,19
- Increasing inspired oxygen concentration by administering 100% oxygen during the procedure.19,23
- When using general anesthesia, decreasing the concentration of volatile agent prior to prosthesis insertion.2,23
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- Utilizing invasive hemodynamic monitoring when pre-existing cardiopulmonary problems exist and during cementing.\(^1,19,23\)

- Providing drug administration through a CVP catheter to provide access to the central circulation, improve coronary perfusion, and maintain cardiac output.\(^6\)

Surgical Techniques

- Patient Condition

  - In the presence of pre-existing cardiopulmonary dysfunction, avoiding bilateral hip replacements with cemented prostheses\(^23\) and using non-cemented prostheses may prevent cardiovascular instability.\(^1,18,20,23\)

  - During the procedure, if the patient’s mean arterial pressure decreases by 20 to 30% below baseline during canal reaming or plugging, changing the technique from cemented to uncemented prosthesis to minimize embolic load.\(^1,19\)

- Lavage

  - Conducting thorough, pulsatile, high pressure, high-volume lavage and brushing and drying of the intramedullary canal of the femoral shaft to remove tissue prior to cement insertion reduces disturbances in pulmonary function and prevents microembolization of marrow contents and the embolic response, thereby reducing the risk of fat embolism and minimizing circulatory changes.\(^1,3,11,15,19,23,27\)

- Venting Hole

  - For long-stem prostheses, using a venting hole in the distal femur reduces distal trapping of debris and reduces pressurization by creating intramedullary drainage.\(^1,3,5,11,15,19,21\)

  However, drilling a venting hole may reduce the prosthesis stability or increase the risk of fracture.\(^2\)

- Cement Restrictor/Plug

  - Using a cement restrictor may cause less physiological disturbance.\(^17\) The restrictor may help compartmentalize marrow, fat, debris, and blood, reducing the risk of BCIS,\(^3,28\) particularly if combined with other methods to reduce intramedullary pressures (e.g., a venting hole). However, for some high-risk patients, the surgeon may wish to avoid increased femoral pressurization that might occur with the sole use of a restrictor.\(^1\)

-Cement Preparation

- Before insertion, working the cement to remove volatile vasodilator compounds.\(^23\)

- Mixing bone cement in a vacuum.\(^10\)

- Using low viscosity cement to reduce intramedullary canal pressures.\(^21\)

- Insertion

  - Using a cement gun to apply the cement under sustained low pressure, thus avoiding excessive cement pressurization.\(^1,11,19\) The retrograde cement gun technique provides more even pressure distribution and less pressure of residual debris than finger packing of cement\(^7\) and is less likely to negatively impact physiological parameters.\(^3,21\)

  - Slowly introducing the prosthesis stem into the cemented femoral canal reduces pressurization, as well.\(^19\) Implant insertion produces maximum pressure, not cement insertion.\(^3\)

  - Some surgeons have used vacuum along the linea aspera to drain the proximal femur to reduce high intramedullary pressure during cement and prosthesis insertion, thus reducing migration of bone marrow and fat into the venous system.\(^24\)

Parvizi et al. reported that many of these risk reduction strategies reduced the overall mortality rate more than 3.5 times from the first study period (1969 to 1988) to the second study period after these changes were implemented (1988 to 1997) (p<0.05).\(^1\) This suggests that intraoperative death associated with hip arthroplasties can be reduced by interventions related to patient assessment, patient selection, intraoperative fixation techniques, and improved monitoring and anesthesia management,\(^1\) including an immediate resuscitation protocol based on the pathophysiology of right ventricular failure.\(^2\)

Treatment

BCIS may be reversible with prompt basic life support, combined with treatment to maintain both coronary perfusion pressure and right heart function.\(^14\) An anesthesiologist ordinarily manages this intervention of supporting the cardiovascular system, treating right heart failure, administering 100% oxygen, and maintaining aggressive volume support. Quick initiation of hemodynamic monitoring is helpful in light of the potential for severe pulmonary
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Self-Assessment Questions

The following questions about this article may be useful for internal education and assessment. You may use the following examples or come up with your own.

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1. Symptoms of bone cement implantation syndrome (BCIS) may include:
   A. Cardiac dysrhythmia/arrhythmia, hypotension, death
   B. Cardiac dysrhythmia/arrhythmia, hyperthermia, death
   C. Inflammation, pain, cellulitis
   D. Fracture, neurological impairment, osteoporosis

2. The underlying causes of BCIS symptoms include:
   A. Endocrine imbalance and erratic blood glucose control
   B. Liver and renal failure
   C. Sepsis and malignant hyperthermia
   D. Right ventricular failure and hemodynamic effects of medullary fat embolus

3. Usually BCIS symptoms occur during or within minutes of cementing the prosthesis.
   A. True
   B. False

4. BCIS risk factors include:
   A. Diseases that compromise the immune system
   B. Hypovolemia and pre-existing cardiac problems
   C. Multiple sclerosis and Parkinson’s disease
   D. Diabetes mellitus and low serum albumin

5. BCIS-specific risk reduction strategies include all but:
   A. Postponing arthroplasty until patient’s cardiac condition is stabilized
   B. Controlling intramedullary pressure
   C. Performing uncemented procedures in high-risk patients
   D. Labeling all basins, bowls, cups, and syringes used intraoperatively

hypertension and impaired cardiac output. Early placement of a pulmonary artery catheter allows use of pulmonary vasodilators, in addition to assessment of positive end-expiratory pressure levels in extreme circumstances. When cement is first introduced into the femoral shaft and for about ten minutes thereafter, the anesthesiologist must be cautious about conducting anesthesia until the patient’s arterial blood pressure spontaneously returns to its initial level.

When symptoms of BCIS occur, the anesthesiologist can administer fluid volumes to augment right ventricular preload. When CVP monitoring indicates large increases in central venous pressure, the anesthesiologist can cease fluid loading. Direct-acting vasopressors, such as phenylephrine or norepinephrine, can be titrated to restore adequate aortic perfusion. This process combats right ventricular ischemia and improves right ventricular function.

To improve contractility and ventricular function, anesthesia can administer inotropes, such as dobutamine, provided there is adequate right ventricular perfusion pressure to meet the increased oxygen demand caused by these agents. Isoproterenol can be beneficial if the patient has adequate perfusion pressure, even though it causes vasodilation. If perfusion pressure is inadequate, isoproterenol can cause further hypotension and deterioration in the patient’s condition.

The above interventions to restore right ventricular function must be initiated immediately when symptoms of embolization occur (e.g., reduced SaO2, reduced PETCO2, tachycardia, bradycardia).

If this syndrome does not result in sudden cardiac death, it may persist for several hours. BCIS is a time-limited process. Both human and animal studies indicate that pulmonary artery pressures normalize within 24 hours. Healthy hearts can recover within minutes, even from large embolic loads associated with cemented implantation. BCIS is reversible even in elderly, critically ill patients, if their hemodynamic stability is maintained by supportive therapy. Therefore, it is essential to immediately identify BCIS and institute aggressive measures in the operating room that address the right ventricular ischemia and failure.

The ability to tolerate embolic load is related to the heart’s ability to maintain adequate right ventricular output during increased pulmonary vascular resistance. A key factor in maintaining cardiac output during and after embolization is the ability to increase the heart rate in the presence of decreased stroke volume.

Notes

5. Orsini EC, Byrick RJ, Mullen JBM, et al. Cardiopulmonary

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Methyl Methacrylate

Methyl methacrylate (MME) is commonly found in healthcare facilities in surgical bone cement. It is a volatile, colorless liquid that has a strong, sharp, distinctive odor. It is an irritant to eyes, skin, mucous membranes, and the respiratory system. Occupational health risks from MME are mainly associated with breathing the vapors and handling the bone cement; however, it also poses explosion and fire risks (see below). MME remains in use because it forms a strong, hard polymer that bonds tightly to many other substances.

MME presents a fire hazard. When exposed to an ignition source (e.g., a Bovie), it can produce acetylene, which is an extremely flammable gas. Above the flash point (50°F), MME vapor-air mixtures can be explosive. Vapors are heavier than air and may flow to a distant ignition source and flash back.

Before working with MME, refer to the its Material Safety Data Sheet to learn of its properties, hazards, health effects, as well as requirements for storage and handling and measures for first aid, fire fighting, accidental release, exposure controls, and personal protection. Also, implement safe practices related to labeling of containers holding MME and its components, to ensure that this product is used as intended in the operative setting.

Sources
The Patient Safety Authority is an independent state agency created by Act 13 of 2002, the Medical Care Availability and Reduction of Error ("Mcare") Act. Consistent with Act 13, ECRI, as contractor for the PA-PSRS program, is issuing this newsletter to advise medical facilities of immediate changes that can be instituted to reduce serious events and incidents. For more information about the PA-PSRS program or the Patient Safety Authority, see the Authority’s website at www.psa.state.pa.us.

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