

The incidence of acute cardiorespiratory and vascular dysfunction following intramedullary nail fixation of femoral metastasis

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ABSTRACT – Intramedullary nail fixation is a common treatment for metastatic tumors of the femur with overt or impending femoral fracture. This procedure sometimes causes severe cardiorespiratory and vascular dysfunction. The clinical relevance of this is not clear. We reviewed 45 operations in 43 patients, where intramedullary nail fixation was used to treat metastatic femoral fractures and impending fractures. We studied the incidence of intraoperative oxygen desaturation and hypotension associated with intramedullary manipulation as markers of cardiorespiratory and vascular dysfunction. Acute oxygen desaturation and hypotension occurred in 11 of our 45 patients. Of these, 3 died, 2 required intensive care postoperatively and 6 made uneventful recoveries. We hope to highlight a serious complication in this patient group.

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The syndrome of acute systemic hypotension, pulmonary hypertension, oxygen desaturation and occasionally cardiac arrest is a well recognized complication associated with manipulation and pressurization of the femoral canal in procedures such as hip arthroplasty and intramedullary fixation of femoral fractures (Kerr et al. 1993, Fitzgerald et al. 1994, Enneking 1995, Lewis 1997). This syndrome appears to be associated with the release of embolic particles (Pell et al. 1993, Duwelius et al. 1997, Lafont et al. 1997), as well as vasoactive, inflammatory and thrombogenic substances from the intramedullary canal (Baker et al. 1971, Modig et al. 1975, Malik 1983,

Strecker et al. 1993, Fujimura et al. 1995, Dahl 1997). With regard to the latter, Dahl (1997) suggests that fat in the lung capillaries may be an epiphenomenon and that the bone trauma and subsequent thrombin generation are probably an important trigger of cardiorespiratory and vascular dysfunction. Christie et al. (1995) have documented with transesophageal echocardiography that patients undergoing nailing of pathological fractures have more venous endogenous material than those without metastases undergoing hemiarthroplasty, posttraumatic femoral or tibial intramedullary fixation (Christie et al. 1995).

Several terms have been used to describe the acute, intraoperative, clinical syndrome of systemic hypotension, pulmonary hypertension, hypoxemia, arrhythmia and occasional cardiac arrest associated with intramedullary manipulation and pressurization. The terms 'cement implantation syndrome' (Lafont et al. 1994, Byrick 1997), 'fat embolism' (Baker et al. 1971, Modig et al. 1975, Hall and Callaghan 1994) and 'fat embolism syndrome' (Hagley et al. 1986, Levy 1990, Arroyo et al. 1994) are often used but may be misleading. The term 'cement implantation syndrome' is accurately used in some cases, but the same syndrome may occur in cases where no cement was used (Chastre et al. 1990, Castella et al. 1992). The term 'fat embolism' is not always appropriate, since air (Karachalios et al. 1992), tumor tissue (King and Harmon 1994), bone marrow-thrombus aggregates and activated biochemical products released into the circulation may

Table 1. Distribution of femoral metastases and their relationship to the incidence of cardiorespiratory and vascular dysfunction (CRVD)

Location of metastases	n	Number with CRVD
Proximal	18	6
Multiple	13	3
Midshaft	9	1
Distal shaft	5	1

cause the clinical effects (Modig et al. 1975, Byrick et al. 1991, Strecker et al. 1993, Christie et al. 1995, Fujimura et al. 1995). A previously suggested more neutral term characterizing the syndrome—i.e., cardiorespiratory and vascular dysfunction (CRVD)—is preferable.

We determined the incidence and clinical characteristics of CRVD in 43 patients with femoral metastases, who underwent intramedullary nailing of the femur (45 operations).

Methods

The hospital files and radiographs of all patients who underwent intramedullary nail fixation for femoral metastases between March 1994 and March 1997 were reviewed. There were 17 men and 26 women having a mean age of 64 (39–93) years. 2 women had bilateral disease, giving a total of 45 operations involving intramedullary nailing of femora with metastases. Both bilateral operations were staged: one within 3 days and the other within 16 months. We included patients with impending fractures (n 36) and whose femur had already fractured (n 9). Patients undergoing another procedure at the same time were excluded. The mean length of stay in an acute hospital was 8 (2–34) days. The commonest site for metastases was the proximal femur, one third of these being associated with CRVD (Table 1). Breast carcinoma was the commonest tumor and one third of these were associated with CRVD (Table 2).

The surgical technique of intramedullary nail fixation is well known. Cement was used in 15 cases for widespread disease on radiographs or when specific reinforcement of large lytic lesions was deemed necessary. Nail insertion was per-

Table 2. Histology of femoral metastases and their relationship to the incidence of CRVD

Type of metastasis	n	Number with CRVD
Breast	24	9
Lung	11	1
Prostate	5	—
Others	3	—
Myeloma	2	1

formed immediately after instillation of cement, while the cement was still in its low viscosity state.

Patients received either a general (n 18) or spinal (n 27) anesthetic at the discretion of the anesthesiologist. Those who had general anesthesia inspired an oxygen concentration of 30% while those given spinal anesthesia received supplemental oxygen via a facemask at 6 L/min.

All patients were monitored continuously by electrocardiography (calibrated lead V5) and pulse oximetry (index finger). Blood pressure was monitored by either an automated non-invasive blood pressure cuff at 3-minute intervals (n 38) or by continuous, direct, intraarterial measurement via a 20-gauge cannula in the radial artery (n 8). End tidal carbon dioxide was monitored in all cases. All parameters were continuously displayed on the anesthetic monitor and charted manually by the anesthesiologist at 5-minute intervals.

Cardiorespiratory and vascular dysfunction

CRVD was defined as an acute intraoperative episode of a decrease in oxygen saturation of 3% and/or a decrease in systolic arterial blood pressure of ≥ 30 mm hg. This had to be simultaneous with intramedullary manipulation. The first author and a senior anesthesiologist in our institution reviewed the medical records independently.

Anticoagulation

All patients received subcutaneous calcium heparin 5000 u at the time of surgery. This was then repeated at 12 hour intervals for the remainder of the hospital stay.

Table 3. 11 patients (12 episodes) with cardiorespiratory and vascular dysfunction

Case Number	% Oxygen desaturation	Hypotension (mmHg)	Cement use	Timing of desaturation	Cardiac arrest
3	27	30	yes	cementation	no
11	7	0	no	reaming	no
17	4	30	no	reaming	no
19	12	0	yes	reaming	no
25	9	110	no	reaming	yes
30	3	120	no	reaming	yes
37	6	0	yes	nail insertion	no
40	7	0	yes	cementation	no
43	12	0	yes	nail insertion	no
44	6	30	yes	reaming	no
45	9 + 4	40 + 30	yes	reaming + cementing	yes

Results

Cardiorespiratory and vascular dysfunction

Episodes of CRVD occurred in 11 of 45 cases and twice in 1 case giving a total of 12 episodes (Table 3). The median desaturation was 8 (3–27)%. Of the 11 patients in whom acute oxygen desaturation occurred, 3 died, 2 had prolonged and intensive-care hospital stays and 6 had uneventful postoperative recoveries. 2 other deaths occurred in patients where the operation was uncomplicated and both were related to postoperative respiratory sepsis. Autopsy was refused in the latter 2 cases.

A decrease in systolic arterial blood pressure was recorded in all 12 episodes of desaturation. However, in only 6 cases (7 episodes) of these 12 episodes were our criteria for reportable hypotension met (mean drop 56 (30–120) mm Hg) (Table 3). Episodes of decreases in systolic arterial blood pressure that met our criteria for intraoperative systemic hypotension also occurred in 1 case where no oxygen desaturation was recorded; it was due to hypovolemia. Deaths occurred in 3 of the 6 cases in whom systolic hypotension was associated with oxygen desaturation.

Reaming of the femoral canal was associated with CRVD in 7 of the 45 cases. Cementation before nail insertion was used in 15 of the 45 cases and in 3 of these 15 cases, oxygen desaturation occurred during the cement pressurization and in another 2 cases, oxygen desaturation occurred during nail insertion after cementation (Table 3). In 1 case, oxygen desaturation occurred during reaming and again during cement pressurization. There were no cases of oxygen desaturation with

or without hypotension, during nail insertion in cases that were not cemented.

Chest radiography

A review of the chest radiographs showed that of the 11 cases in which episodes of oxygen desaturation and hypotension were detected, 5 radiographs were normal, 3 had moderate abnormalities, as evidenced by primary or multiple secondary lung tumors with or without small pleural effusions, and 3 had evidence of severe lung disease, with combinations of multiple metastases, moderate-to-large pleural effusions, lymphangitis carcinomatosa and pulmonary atelectasis. 2 of these 3 patients with severe disease were dependent on supplemental home oxygen prior to admission and all 3 died. Of the 34 patients who did not experience intraoperative complications, 18 had normal chest radiographs, 18 had moderate abnormalities and 1 had severe lung disease. None was dependent on supplemental home oxygen.

Autopsy

Postmortem examination was available only in one case and this confirmed multiple fat and tumor emboli, not only throughout the lung but also in the cerebral parenchyma. There was no cardiac defect that allowed a shunt.

Discussion

Our study shows that intramedullary fixation of femoral metastases is associated with a high inci-

dence of CRVD. The mortality from these episodes was high. Half of our patients who were suspected of having severe CRVD required intensive perioperative treatment; half of them died. Kerr et al. (1993) reported similar results in a series of 23 patients undergoing intramedullary nailing for femoral metastases.

The proportion of cases having CRVD who are reported during intramedullary femoral manipulation depends on the criteria and methods used to define and detect them, respectively. The highest reported proportions of emboli detected during intramedullary manipulation are not in studies using clinical parameters for detection such as ours, but are in studies using intraoperative transesophageal echocardiography or intravascular ultrasound (Ereth et al. 1992, Pell et al. 1993, Lafont et al. 1994, Duwelius et al. 1997). The relationship between the emboli detected by these sensitive techniques and CRVD is unclear. Lafont et al. (1994) reported emboli in 47 of 48 patients undergoing cemented total hip joint replacement using transesophageal echocardiography, but found no correlation between incidence and size of emboli particles, demography or blood gas on hemodynamic variables studied at the same times. Many of his patients remained asymptomatic and no deterioration in mean hemodynamic variables was observed (Lafont et al. 1994). Pell et al. (1993), however, reported that large emboli (> 10 mm) had a more serious clinical effect than showers of small emboli.

Some factors specific to patients with cancer may increase the serious clinical effects of these emboli. Tumor angiogenesis in the femur increases local bone vascularity and increases the risk of emboli gaining access to the venous system (Barre et al. 1997). Pulmonary metastatic disease will further reduce cardiopulmonary reserve. Among our 3 cases who died, all appeared to have more extensive respiratory disease than most of the others. Preoperative pulmonary function tests might have helped to assess their suitability for intramedullary fixation.

While an acute drop in intraoperative peripheral oxygen saturation and associated intraoperative hypotension may be relatively nonspecific and result from other causes, we chose these indices to detect cases of CRVD. The pulse

oximeter has been previously validated as a useful method for finding clinically significant yet silent hypoxia and is useful in detecting pulmonary emboli (Moed et al. 1993). To increase the likelihood that these measures indicate significant CRVD, we relied on the simultaneous occurrence of oxygen desaturation, systolic hypotension and intramedullary manipulation and excluded other causes.

Christie et al. (1995) have correlated intraoperative oxygen saturation with severity of the embolic phenomena, as measured by transesophageal echocardiography. The mean intraoperative fall in oxygen saturation during severe embolism was 2.9%. In this study, we used a reduction in oxygen saturation of 3% or more as a marker of a pulmonary embolic event. Given the inspired supplemental oxygen, this would require an increase in shunt or pulmonary venous admixture from 5–30% before a change is detected and we believe that this would correspond to a large pulmonary circulatory change. While our study should estimate the incidence of clinically significant pulmonary embolic events, it clearly underestimates the incidence of all CRVD.

The reported risk of systemic hypotension, following manipulation and pressurization of the femoral canal, is highly variable—i.e., from 5–50% (Pietak et al. 1997). In our study, the percentage of cases having intraoperative hypotension was approximately 20%. A mortality rate of 10% following hypotensive episodes has been reported (Duncan 1989) and our study indicates that it may be higher.

Reaming was associated with acute oxygen desaturation in approximately 1/6 of cases. The relationship between reaming, cement insertion and nail insertion to CRVD remains unclear. Some authors have suggested that CRVD is related to surgical techniques, such as opening the intramedullary canal with an awl, the first two passes of the reamer and the insertion of the nail (Duwelius et al. 1997, Pietak et al. 1997). Intramedullary pressures of 750–1126 millimeters of mercury have been recorded during reaming (Hughes et al. 1993, Muller et al. 1993, Wozasek et al. 1994) and although these pressures have not been reported with unreamed nails, it appears that reaming pressures can be lowered to those of unreamed

nails with improved techniques (Muller et al. 1993, Peter et al. 1993). However, unreamed nail insertion does not seem to offer protection (Heim et al. 1993, 1995, Neudeck et al. 1996, Duwelius et al. 1997). Pulsatile lavage of the intramedullary canal to remove tissue and vasoactive products reduces emboli (Sherman et al. 1983, Byrick et al. 1989, Wheelwright et al. 1993). Flexible, small-diameter drive shafts appear to allow a path of low resistance for the intramedullary contents to escape up the femoral canal (Muller et al. 1993).

One third of our patients developed acute oxygen desaturation when nail insertion was combined with cementation. The benefits of cement are that it gives additional strength (Harrington et al. 1976, Harrington 1997) in femora with widespread disease or large lytic lesions. The harmful effects of methylmethacrylate are well documented in the literature (Ware et al. 1991, Pinto 1993, Propst et al. 1993, Fujimura et al. 1995). The important effect of cement may be to seal the femoral shaft and increase intramedullary pressure more during pressurization and nail or prosthesis insertion than is usually encountered (Pietak et al. 1997).

The treatment of these pulmonary embolic events is essentially supportive. For this reason, anesthetic prophylaxis appears to be paramount. The Anesthetic Advisory Committee to the Chief Coroner of Ontario stressed that some anesthesiologists may not recognize the event or patients at risk, and have no resuscitation protocol to deal immediately with the problem (Pietak et al. 1997). They emphasized the importance of normovolemia, increased inspired oxygen concentrations and decreased volatile agent concentration, prior to prosthesis insertion (Pietak et al. 1997). The use of direct-acting vasopressors, such as norepinephrine or phenylephrine, to achieve adequate aortic perfusion pressure is recommended (Molloy et al. 1984, Vlahakes et al. 1981). Dahl (1997) suggests that the circulatory and respiratory effects observed may be due to the hormonal action of thrombin on the pulmonary circulation. In this regard, bone trauma activates the hemostatic system and fibrin is formed in the lung vessels, with trapping of cellular debris. Dahl postulates that the use of low molecular weight heparin and dextran 70 may modify this process.

Our study emphasizes the substantial morbidity and mortality of oxygen desaturation and hypotension in patients undergoing intramedullary fixation of femoral metastasis. We consider that much of this is intimately associated with pulmonary embolic events. To reduce this risk, we now routinely test pulmonary function preoperatively to assess suitability for this procedure, to monitor end tidal carbon dioxide and use invasive blood pressure monitoring to assist us in early detection and management. While we acknowledge the limitations of a retrospective study, we hope to highlight a finding we consider important and promote further attention to this procedure, which is often performed by inexperienced and unsuspecting staff.

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