

Bone cement implantation syndrome in cemented hemiarthroplasty for femoral neck fracture: incidence, risk factors, and effect on outcome

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Editor's key points

- Bone cement implantation syndrome (BCIS) is well recognized in orthopaedic surgery, but its incidence is unclear.
- In this study of patients undergoing hemiarthroplasty, the overall incidence of BCIS was 28%.
- Both 30 day and long-term mortality were significantly higher after a moderate or severe episode of BCIS.
- These data support increased vigilance and preventive measures during cement implantation.
- Alternatives to cemented prostheses should perhaps be considered in patients at high risk of BCIS.

Background. Bone cement implantation syndrome (BCIS) is characterized by hypoxia, hypotension, and loss of consciousness occurring around the time of bone cementation. Using a recently proposed severity classification of BCIS, we estimated the incidence of and risk factors for BCIS and its impact on mortality in cemented hemiarthroplasty for femoral neck fractures.

Methods. In this retrospective study, 1016 patients undergoing cemented hemiarthroplasty were included. Medical history and medication were obtained from medical records. Anaesthesia charts for all patients were reviewed for mean arterial pressure, arterial oxygen saturation, and heart rate before, during, and after cementation. Each patient was classified as having no BCIS (grade 0) or BCIS grade 1, 2, or 3, depending on the degree of hypotension, arterial desaturation, or loss of consciousness around cementation.

Results. The incidence of BCIS grade 1, 2, and 3 were 21%, 5.1%, and 1.7%, respectively. Early mortality in BCIS grade 1 (9.3%) did not differ significantly from BCIS grade 0 (5.2%), while early mortality in BCIS grade 2 (35%) and grade 3 (88%) were significantly higher when compared with grades 0 and 1. Early mortality was also higher in BCIS grade 3 when compared with grade 2. Independent predictors for severe BCIS were: ASA grade III–IV, chronic obstructive pulmonary disease, and medication with diuretics or warfarin. Severe BCIS was associated with 16-fold increase in mortality.

Conclusions. BCIS is a commonly occurring phenomenon in cemented hemiarthroplasty and severe BCIS has a huge impact on early and late mortality.

Keywords: bone cement implantation syndrome; femoral neck fracture; hemiarthroplasty; outcome; risk factors

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Bone cement implantation syndrome (BCIS) is a well known and potentially fatal complication of orthopaedic surgery involving pressurized bone cement.¹ The syndrome is most often seen in cemented hemiarthroplasty but also occurs in total hip replacement and knee replacement surgery. The syndrome is characterized by hypoxia,^{2,3} sudden loss of arterial pressure,^{3,4} pulmonary hypertension,^{4,5} arrhythmias,⁶ loss of consciousness, and eventually cardiac arrest.^{7,8}

The pathophysiology of BCIS is not entirely clear. Anaphylaxis,⁹ inflammatory, thermic, and complement activation¹⁰ have all been thought to play a role. Studies involving invasive haemodynamic monitoring and perioperative ultrasound have revealed a large degree of subclinical pulmonary embolisms^{5,11} and

haemodynamic effects not seen in standard perioperative monitoring.¹²

In cemented total hip arthroplasty, the incidence of intraoperative death is 0.11% and mortality occurs around the time of cementation.¹ In a study including patients with and without hip fractures, the intraoperative mortality for cemented hemiarthroplasty is considerably higher (0.43%).⁶ In the same study, it was shown that the intraoperative mortality for cemented hemiarthroplasty in patients with hip fractures was 0.2–4.3%, depending on the type of fracture.

The true incidence of BCIS in cemented hemiarthroplasty for hip fractures is, however, not known mainly because this syndrome has, until recently, not had an agreed standard

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definition. Donaldson and colleagues¹ recently proposed a severity classification of BCIS: grade 1 was defined as moderate hypoxia (arterial oxygen saturation $<94\%$) or hypotension [a decrease in systolic arterial pressure (SAP) $>20\%$], grade 2 as severe hypoxia (arterial oxygen saturation $<88\%$) or hypotension (a decrease in SAP $>40\%$) or unexpected loss of consciousness, and finally, grade 3, which was defined as cardiovascular collapse requiring cardiopulmonary resuscitation.

The aim of the present study was to estimate the incidence of BCIS in cemented hemiarthroplasty for hip fractures, using this severity classification of BCIS. Furthermore, we wanted to elucidate the risk factors for the development of this syndrome and the impact of BCIS for early (30 days) and late (1 yr) mortality.

Methods

The study was approved by the Ethics Committee of the University of Gothenburg and written informed consent was waived by the Ethics Committee. In this retrospective cohort study, the medical records of all consecutive patients undergoing cemented hemiarthroplasty for femoral neck fracture from January 1, 2008 to June 30, 2011 at Sahlgrenska University Hospital/Mölndal were reviewed.

Medical history, medication, and baseline data were obtained from the medical records. In addition to age, BMI, gender, current drug therapy, history of smoking, and ASA risk score, we collected data regarding preoperative cardiac history and presence of coexisting diseases, including liver disease, renal impairment (serum creatinine $>150 \mu\text{mol litre}^{-1}$), diabetes mellitus, previous stroke, peripheral vascular disease, hypertension, chronic obstructive pulmonary disease (COPD), cancer, dementia, and arrhythmias. Furthermore, intraoperative data on blood loss, length of surgery, and type of anaesthesia (regional or general) were obtained.

The anaesthesia charts of all patients were reviewed for mean systolic pressure, arterial oxygen saturation, and heart rate. At our institution, these variables are recorded immediately before induction of anaesthesia and every fifth minute during the operation. Data on systolic arterial pressure, heart rate, and arterial oxygen saturation were obtained at four occasions: (i) immediately before induction of anaesthesia, (ii) every fifth minute, for a period of 10–15 min before implantation of bone cement, (iii) every fifth minute, for a period of at least 15 min after implantation of bone cement, and (iv) on arrival to the post-anaesthesia recovery unit. The lowest SAP recorded within 15 min after cementation was used to score the severity of BCIS. Non-invasive cardiac output monitoring was not used in any patient. Each patient was classified as having no BCIS (grade 0) or grade 1, 2, or 3 BCIS, according to Donaldson and colleagues.¹

Statistical analysis

The Kaplan–Meier methods were used to compare postoperative mortality between patients without and with various grades of BCIS. Comparisons of postoperative survival between groups were performed with a log-rank (Mantel–Cox) test.

A two-tailed P -value of <0.05 was considered significant. The patients were dichotomized according to their individual BCIS score to: Group 1, constituted by patients with no (grade 0) or moderate (grade 1) and Group 2 constituted by patients with severe BCIS (grade 2 or 3). Univariate correlates for the development of severe BCIS, between baseline and intraoperative characteristics, were tested using the unpaired t -test for continuous variables and the χ^2 test or Fisher's exact test for dichotomous data (Table 1). Independent predictors of baseline and intraoperative variables for the development of severe BCIS were assessed by a stepwise multiple logistic regression. For each variable, the odds ratio (OR) and its 95% confidence intervals (CIs) were calculated. Predictors with an OR <0.5 , >2.0 or $P<0.05$ were finally included in the stepwise logistic regression analysis. To evaluate the role of BCIS and other independent predictors of 30 day mortality, univariate and binomial multivariate regression analyses were performed. Data are presented as ORs and its 95% CI.

Results

One thousand and eighty patients were enrolled for review of medical records. Thirty-three cases were excluded due to erroneous classification in the surgical registry ($n=30$) or because of lack of perioperative documentation ($n=3$). Another 31 patients receiving cemented hemiarthroplasty for other indications than acute hip fracture were also excluded. After exclusions, 1016 cases operated with cemented hemiarthroplasty due to displaced fracture of the femoral neck were included for analysis.

The all-cause 30 day and 1 yr mortality were 9% and 29%, respectively. All-cause perioperative mortality, defined as death within 48 h after surgery, was 2.0%. The total incidence of BCIS regardless of severity was 283/1016 (28%). The incidence of BCIS grades 1, 2, and 3 were 21%, 5.1% and 1.7%, respectively. When compared with the group with no symptoms of BCIS, with a 30 day mortality of 5.2%, 30 day mortality for BCIS grades 1, 2, and 3 were 9.3%, 35% and 88%, respectively. Corresponding values for 1 yr mortality were 25.2% (grade 0), 29.9% (grade 1), 48.1% (grade 2), and 94.1% (grade 3), respectively. The impact of BCIS on cumulative survival is shown in Figure 1. Pairwise comparisons using the log-rank test showed that mortality in BCIS grade 1 did not differ significantly from BCIS grade 0 ($P=0.15$), while mortality in BCIS grades 2 and 3 were significantly higher when compared with grade 0 ($P<0.001$ and <0.001 , respectively) and grade 1 ($P<0.009$ and <0.001 , respectively). Mortality was also higher in BCIS grade 3 when compared with grade 2 ($P<0.001$). As there was no significant difference in mortality between BCIS grades 0 and 1, the Kaplan–Meier estimates of pooled data from BCIS grades 0 and 1, and pooled data from grades 2 and 3 are presented in Figure 2. Detailed cumulative 30 day survival data from these two groups are shown in Figure 3. Mortality within 48 h were 0.11% and 28% for BCIS grades 0 and 1 and BCIS grades 2 and 3, respectively. Corresponding data on 30 day mortality were 6% and 47%, respectively.

Table 1 Baseline characteristics. Age is presented as mean (min–max). Preoperative haemoglobin, serum creatinine, and BMI are expressed as mean (range). Renal failure is defined as serum creatinine $>150 \mu\text{mol litre}^{-1}$. Diabetes includes both types I and II. BCIS, bone cement implantation syndrome; ACE, angiotensin-converting enzyme. Categorical data were compared using the χ^2 test or Fisher's exact test for dichotomous data and the unpaired *t*-test were used for continuous variables

| | BCIS grade 0 or 1 (n=947) | BCIS grade 2 or 3 (n=69) | P-value |
|---|---------------------------|--------------------------|---------|
| Age | 84 (57–100) | 86 (74–99) | NS |
| BMI | 23.6 (4.1) | 23.2 (5.6) | NS |
| Regional anaesthesia | 822 (87%) | 59 (86%) | NS |
| Gender | | | |
| Male | 272 (28.7%) | 21 (30.4%) | NS |
| Female | 675 (71.3%) | 48 (69.6%) | NS |
| ASA classification | | | |
| I | 22 (2.3%) | 1 (1.4%) | NS |
| II | 380 (40.1%) | 14 (20.3%) | <0.05 |
| III | 506 (53.4%) | 42 (60.9%) | NS |
| IV | 39 (4.1%) | 12 (17.4%) | <0.05 |
| Medical history | | | |
| Liver disease | 11 (1.2%) | 0 (0%) | NS |
| Renal failure | 58 (6.1%) | 6 (8.7%) | NS |
| Diabetes | 122 (12.9%) | 13 (18.8%) | NS |
| Stroke | 173 (18.3%) | 14 (20.3%) | NS |
| Peripheral arterial disease | 25 (2.6%) | 1 (1.4%) | NS |
| Arteriosclerosis | 18 (1.9%) | 4 (5.8%) | NS |
| Hypertension | 384 (40.5%) | 33 (47.8%) | NS |
| Angina pectoris | 125 (13.2%) | 16 (23.2%) | 0.029 |
| Previous myocardial infarction | 103 (10.9%) | 10 (14.5%) | NS |
| Congestive heart failure | 100 (10.6%) | 13 (18.8%) | 0.045 |
| Chronic obstructive pulmonary disease | 110 (11.6%) | 16 (23.2%) | 0.012 |
| Cancer | 70 (7.4%) | 4 (5.8%) | NS |
| Dementia | 250 (26.4%) | 15 (21.7%) | NS |
| Arrhythmia | 203 (21.4%) | 22 (31.9%) | NS |
| Medication | | | |
| β -Blockers | 339 (35.8%) | 38 (55.1%) | 0.005 |
| Diuretics | 335 (35.4%) | 40 (58%) | 0.005 |
| Antiplatelet drugs | 404 (42.7%) | 32 (46.4%) | NS |
| Organic nitrates | 128 (13.5%) | 14 (20.3%) | NS |
| Calcium antagonists | 192 (20.3%) | 8 (11.6%) | NS |
| ACE inhibitors | 211 (22.3%) | 26 (37.7%) | 0.005 |
| Insulin | 60 (6.3%) | 7 (10.1%) | NS |
| Warfarin | 55 (5.8%) | 12 (17.4%) | 0.005 |
| Statins | 130 (13.7%) | 11 (15.9%) | NS |
| Preoperative haemoglobin (g litre $^{-1}$) | 125 (15) | 127 (13) | NS |
| Serum creatinine ($\mu\text{mol litre}^{-1}$) | 85 (41) | 93 (41) | NS |

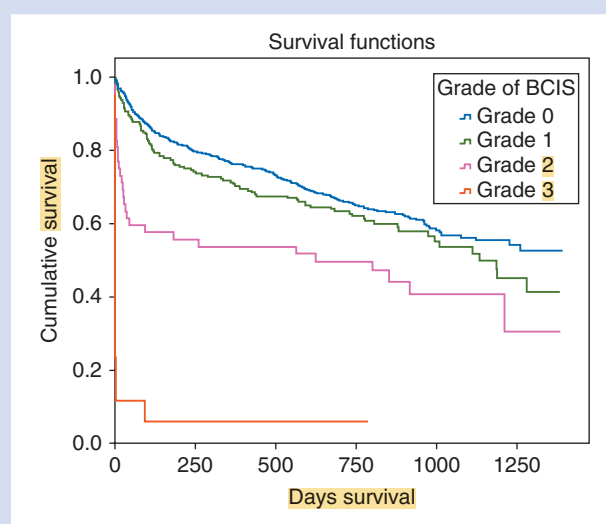


Fig 1 Cumulative long-term survival after cemented hemiarthroplasty for femoral neck fracture in relation to grade of BCIS. The Kaplan–Meier methods and the log-rank (Mantel–Cox) were used to compare postoperative mortality between patients without and with various grades of BCIS. Survival in BCIS grade 1 did not differ significantly from BCIS grade 0 ($P=0.15$), while survival in BCIS grades 2 and 3 was significantly lower when compared with grade 0 ($P<0.001$ and <0.001 , respectively) and grade 1 ($P<0.009$ and <0.001 , respectively). Survival was also lower in BCIS grade 3 when compared with grade 2 ($P<0.001$).

When evaluating risk factors for the development of BCIS, the material was dichotomized as described above. In Table 2, it can be seen that patients developing severe BCIS (grade 2 or 3) had significantly higher ASA classification ($P<0.05$), a higher incidence of angina pectoris ($P=0.029$), congestive heart failure (CHF) ($P=0.045$), and COPD ($P=0.012$) compared with those with no or moderate BCIS (grade 0 or 1). Furthermore, the use of β -adrenergic blockers ($P<0.005$), diuretics ($P<0.005$), angiotensin-converting enzyme inhibitors ($P=0.005$), and warfarin ($P<0.005$) was more frequent in patients developing severe BCIS.

Perioperative blood loss was 327 (238) ml in patients with no or moderate BCIS compared with 301 (191) ml in patients with severe BCIS (NS). The duration of surgery was 87 (27) min in patients with no or moderate BCIS and 84 (26) min in patients developing severe BCIS (NS). Surgery was performed with regional anaesthesia in 87% and 86% of the patients in the two groups, respectively (NS).

The unadjusted and the adjusted ORs for development of severe BCIS are shown in Table 3. Independent predictors for development of severe BCIS were, ASA grades III–IV (OR 2.0; 95% CI, 1.1–3.6), pre-existing COPD (OR 2.0; 95% CI, 1.1–3.8), and medication with diuretics (OR 1.9; 95% CI, 1.2–3.2) or warfarin (OR 2.7; 95% CI, 1.4–5.5).

Predictors and ORs for 30 day mortality are shown in Table 3. After adjusting for confounding factors, independent risk factors for 30 day mortality after cemented hemiarthroplasty were, age over 85 yr (OR 2.2; 95% CI, 1.3–3.8), male gender

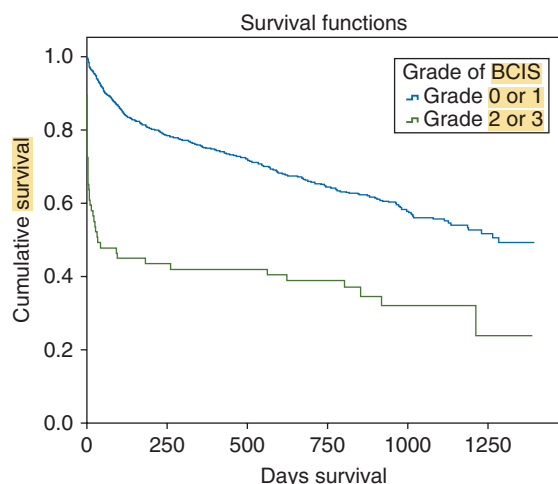


Fig 2 Cumulative long-term survival after cemented hemiarthroplasty for femoral neck fracture in relation to grade of BCIS. Patients were dichotomized into two groups: the first group had BCIS grade 0 or 1 (blue), while the second group had BCIS grade 2 or 3 (green). The Kaplan–Meier methods and the log-rank (Mantel–Cox) were used to compare postoperative mortality between the two groups. Survival was lower in patients with more severe forms of BCIS ($P < 0.005$).

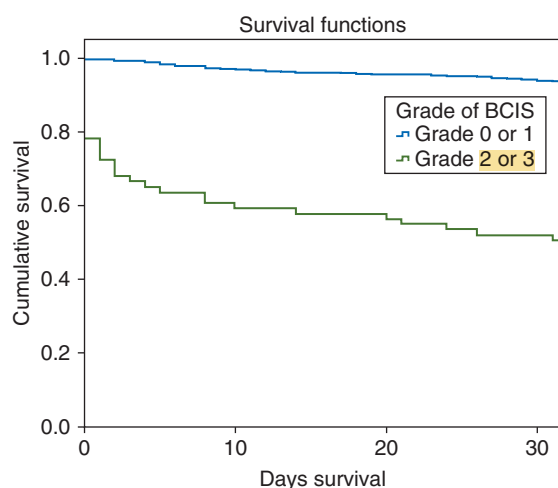


Fig 3 Detailed cumulative 30 day survival after cemented hemiarthroplasty for femoral neck fracture in relation to grade of BCIS. Patients were dichotomized into two groups: the first group had BCIS grade 0 or 1 (blue), while the second group had BCIS grade 2 or 3 (green). The Kaplan–Meier methods and the log-rank (Mantel–Cox) were used to compare postoperative mortality between the two groups. Early survival was lower in patients with more severe forms of BCIS ($P < 0.005$).

(OR 2.0; 95% CI, 1.2–3.2), CHF (OR 1.91; 95% CI, 1.0–3.64), dementia (OR 2.81; 95% CI, 1.67–4.74), and medication with diuretics (OR 1.95; 95% CI, 1.17–3.26). Development of

intraoperative severe BCIS (grade 2 or 3) was associated with 16-fold increase in odds of 30 day mortality compared with those who did not develop BCIS or those who developed moderate BCIS (grade 1) (OR 16.4; 95% CI, 8.84–30.24).

Discussion

To our knowledge, this is the first study using the classification system for BCIS proposed by Donaldsson and colleagues,¹ to describe the incidence of BCIS and its risk factors and impact on early and late mortality in a large population of patients undergoing cemented hemiarthroplasty for hip fracture. The main findings were that the BCIS, regardless of its severity, is a fairly common complication with an incidence of 25–30% and that, in more severe forms, BCIS confer a 16-fold increase in 30 day postoperative mortality. Furthermore, independent risk factors for the development of the BCIS were high ASA grade, COPD, and medication with diuretics and warfarin.

The reported all-cause 30 day and 1 yr mortality in patients undergoing surgery for hip fractures range from 2.5% to 8%^{13 14} and over 25%,^{15 16} respectively. In a recent study on perioperative mortality after hemiarthroplasty based on the Australian Orthopaedic Association National Joint Replacement Registry, evaluating almost 13 000 patients with cemented hemiarthroplasty, Costain and colleagues¹⁷ showed that 30 day and 1 yr mortality were 7% and 21%, respectively. In the present study, 30 day and 1 yr mortality were somewhat higher, 9% and 29%, respectively. The somewhat higher mortality in the present study could be explained by the higher age in our population of patients compared with that presented in the report by Costain and colleagues. Furthermore, it is not immediately evident, whether or not the latter report only included patients subjected to cemented hemiarthroplasty for hip fracture.

The perioperative mortality in the present study was 2.0% and 95% of the patients who died within 48 h had BCIS grade 2 or 3 during surgery. Previous studies on patients undergoing cemented hemiarthroplasty for femoral neck fracture have demonstrated an all-cause perioperative mortality of 1.3–2.5%.^{17 18} Perioperative mortality is significantly higher after cemented hemiarthroplasty compared with uncemented implant insertions.^{17 18} However, Costain and colleagues showed that at 1 yr after operation, the mortality was reversed with a favourable survival for patients treated with cemented hemiarthroplasty, suggesting that high-risk patients are more likely to succumb in the early perioperative period if bone cement is used. In Figure 3, it can be seen that mortality from cemented hemiarthroplasty is seen intraoperatively and in the immediate postoperative period and thereafter the survival curve of the group of patients experiencing BCIS does not obviously differ from the group of patients not developing BCIS. Thus, efforts should be made to identify patients undergoing cemented hemiarthroplasty for femoral neck fracture, at risk for BCIS, to be able to perform intraoperative preventive measures in order to decrease the risk of developing BCIS and improve survival in these patients.

In the present study, we showed that the more severe form of BCIS the patient developed intraoperatively, according to

Table 2 Predictors and ORs for developing severe BCIS (grade 2 or 3). Renal failure defined as creatinine over 150 $\mu\text{mol litre}^{-1}$. CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; ACE, angiotensin-converting enzyme. Unadjusted ORs were calculated for each variable. Adjusted ORs are presented only for the independent predictors of severe BCIS, assessed by a stepwise multiple logistic regression

| Predictors | Odds ratio (unadjusted) | 95% CI | P-value | Odds ratio (adjusted) | 95% CI | P-value |
|--------------------------------|-------------------------|-----------|---------|-----------------------|-----------|---------|
| Age >85 yr | 0.85 | 0.52–1.39 | 0.535 | | | |
| Male sex | 0.92 | 0.54–1.57 | 0.784 | | | |
| ASA III or IV | 2.65 | 1.48–4.77 | 0.001 | 1.97 | 1.07–3.61 | 0.029 |
| Medical history | | | | | | |
| Renal failure | 1.45 | 0.60–3.50 | 0.44 | | | |
| Diabetes | 1.57 | 0.83–2.96 | 0.195 | | | |
| Stroke | 1.14 | 0.62–2.19 | 0.632 | | | |
| Peripheral vascular disease | | | | | | |
| Arteriosclerosis | 3.18 | 1.04–9.66 | 0.056 | | | |
| Hypertension | 1.34 | 0.82–2.19 | 0.255 | | | |
| Angina pectoris | 1.99 | 1.10–3.58 | 0.029 | | | |
| Previous myocardial infarction | 1.39 | 0.69–2.80 | 0.326 | | | |
| CHF | 1.97 | 1.04–3.72 | 0.045 | | | |
| COPD | 2.30 | 1.27–4.16 | 0.012 | 2.02 | 1.10–3.72 | 0.024 |
| Cancer | 0.77 | 0.27–2.18 | 0.811 | | | |
| Dementia | 0.77 | 0.43–1.40 | 0.478 | | | |
| Arrhythmias | 1.72 | 1.01–2.91 | 0.051 | | | |
| Medication | | | | | | |
| β -Blockers | 2.20 | 1.34–3.60 | 0.002 | | | |
| Diuretics | 2.52 | 1.53–4.14 | <0.0001 | 1.92 | 1.15–3.22 | 0.013 |
| Antiplatelet drugs | 1.16 | 0.71–1.90 | 0.615 | | | |
| Organic nitrates | 1.63 | 0.88–3.01 | 0.147 | | | |
| Calcium antagonists | 0.52 | 0.24–1.10 | 0.085 | | | |
| ACE inhibitors | 2.11 | 1.27–3.51 | 0.005 | | | |
| Insulin | 1.67 | 0.73–3.81 | 0.209 | | | |
| Warfarin | 3.41 | 1.73–6.74 | 0.001 | 2.69 | 1.33–5.43 | 0.006 |
| Statin | 1.19 | 0.61–2.33 | 0.589 | | | |

the severity classification proposed by Donaldson and colleagues,¹ the higher was the early and late postoperative mortality. However, one important finding was that in patients experiencing BCIS grade 1 with moderate hypoxia (oxygen saturation <94% but not <88%) or moderate hypotension (a decrease in SAP >20% but not >40%), early or late mortality was not significantly affected when compared with patients not developing BCIS. Twenty-one per cent of the patients in the present study developed moderate hypoxia or hypotension around the time of bone cementation, thus fulfilling the criteria for BCIS grade 1. One could speculate that moderate hypoxia or hypotension in this group of patients was caused either by a minor degree of pulmonary embolization, not affecting clinical outcome, or that it was caused by hypovolaemia, atelectasis-induced intrapulmonary shunting, or both which can be easily treated and with no major impact on clinical outcome.

The clinical syndrome of BCIS typically occurs at the time of bone cementation and insertion of the prosthesis. The pathophysiology of BCIS is not fully understood, but may be caused by pulmonary embolization, complement activation, and release of histamine, all, which may act in concert to increase

pulmonary vascular resistance, which, if pronounced enough, may cause ventilation/perfusion disturbances with hypoxia, right ventricular failure,^{1 5 19–21} and cardiogenic shock. In a recent intraoperative study, it was shown that cemented hemiarthroplasty in patients with femoral neck fracture indeed causes a pronounced pulmonary vasoconstriction and an impairment of RV function accompanied by pulmonary ventilation/perfusion abnormalities early after cementation and prosthesis insertion.¹²

Independent risk factors for the development of BCIS in the present study were COPD in addition to high ASA score. COPD is often complicated by pulmonary hypertension.²² The mechanisms involved in the pathogenesis of pulmonary hypertension and high pulmonary vascular resistance in COPD are, in addition to hypoxia, acidaemia and destruction of lung parenchyma, likely to be vascular remodelling, inflammation, and endothelial dysfunction.²² The latter mechanisms may alter the responsiveness of the pulmonary vascular bed and may explain why patients with COPD have a higher risk for the development of BCIS. Although the diagnosis of CHF or chronic atrial fibrillation was not itself an independent risk factor for BCIS,

Table 3 Predictors and ORs for 30 day mortality after cemented hemiarthroplasty. Renal failure is defined as serum creatinine $>150 \mu\text{mol litre}^{-1}$. Diabetes includes both types I and II. COPD, chronic obstructive pulmonary disease; ACE, angiotensin-converting enzyme; BCIS, bone cement implantation syndrome. Unadjusted ORs were calculated for each variable. Adjusted ORs are presented only for the independent predictors of 30 day mortality, assessed by a stepwise multiple logistic regression

| Predictors | Odds ratio (unadjusted) | 95% CI | P-value | Odds ratio (adjusted) | 95% CI | P-value |
|---------------------------------------|-------------------------|------------|----------|-----------------------|------------|----------|
| Age >85 yr | 2.21 | 1.41–3.47 | 0.001 | 2.58 | 1.54–4.32 | <0.005 |
| Male sex | 2.08 | 1.34–3.23 | 0.001 | 2.15 | 1.31–3.54 | 0.02 |
| ASA III or IV | 2.85 | 1.69–4.80 | <0.005 | | | |
| Medical history | | | | | | |
| Liver disease | 2.30 | 0.49–10.79 | 0.257 | | | |
| Renal failure | 2.54 | 1.30–4.96 | 0.011 | | | |
| Diabetes | 1.10 | 0.59–2.04 | 0.746 | | | |
| Stroke | 1.19 | 0.70–2.02 | 0.571 | | | |
| Peripheral vascular disease | 0.85 | 0.20–3.64 | 0.999 | | | |
| Arteriosclerosis | 3.12 | 1.12–8.65 | 0.039 | | | |
| Hypertension | 0.72 | 0.46–1.14 | 0.18 | | | |
| Angina | 2.32 | 1.39–3.87 | 0.002 | | | |
| Previous myocardial infarction | 1.51 | 0.82–2.76 | 0.22 | | | |
| Congestive heart failure | 2.50 | 1.46–4.29 | 0.002 | 1.91 | 1.0–3.64 | 0.049 |
| COPD | 1.57 | 0.88–2.80 | 0.133 | | | |
| Cancer | 1.26 | 0.58–2.71 | 0.526 | | | |
| Dementia | 1.89 | 1.21–2.95 | 0.008 | 2.81 | 1.67–4.74 | <0.005 |
| Arrhythmia | 2.15 | 1.37–3.40 | 0.001 | | | |
| Medication | | | | | | |
| β -Blockers | 1.51 | 0.98–2.33 | 0.069 | | | |
| Diuretics | 2.61 | 1.69–4.05 | <0.005 | 1.95 | 1.17–3.26 | 0.012 |
| Antiplatelet drugs | 1.86 | 1.21–2.88 | 0.005 | | | |
| Organic nitrates | 1.86 | 1.09–3.17 | 0.026 | | | |
| Calcium antagonists | 0.72 | 0.40–1.30 | 0.334 | | | |
| ACE inhibitors | 1.27 | 0.78–2.07 | 0.363 | | | |
| Insulin | 0.81 | 0.32–2.07 | 0.826 | | | |
| Warfarin | 1.21 | 0.53–2.72 | 0.656 | | | |
| Statins | 0.84 | 0.43–1.61 | 0.751 | | | |
| Haemoglobin <100 (g litre $^{-1}$) | 1.98 | 0.47–8.34 | 0.575 | | | |
| BCIS grade 2 or 3 | 14.05 | 8.17–24.16 | <0.005 | 16.35 | 8.84–30.24 | <0.005 |

preoperative treatment with diuretics or warfarin was statistically correlated to the development of BCIS. Patients with CHF, particularly if associated with chronic atrial fibrillation, are known to develop pulmonary venous hypertension because of increased left-sided filling pressures.²³

In patients with chronic CHF, pulmonary vascular resistance is elevated because of endothelial dysfunction, with reduced expression of nitric oxide and increased availability of endothelin, and also structural remodelling.²³ One could therefore speculate that patients with COPD and CHF, with or without chronic atrial fibrillation, share common pathophysiological mechanisms, including pulmonary vascular hypereactivity, when exposed to a certain load of pulmonary embolism at the time of bone cementation and insertion of the prosthesis.

The major limitation of the present study is its retrospective nature. In our review, we were therefore limited by the quality of the data presented to us in the medical records of our

institution. The strength of the study includes our efforts to obtain clinical signs of BCIS from the anaesthesia chart of each individual of the included population of more than a thousand patients. We believe that we have identified pre-operative risk factors for the development of severe BCIS. This information could be useful in, for example, future prospective studies evaluating various preventive strategies to limit the risk of BCIS in high-risk patients.

In conclusion, we have, in this retrospective investigation, studied the incidence, risk factors, and the impact on outcome of BCIS in patients undergoing cemented hemiarthroplasty for femoral neck fracture. Regardless of severity, BCIS is a commonly occurring phenomenon in this group of patients with an incidence between 25% and 30%. Severe BCIS occurred in 5–7% of the patients and was associated with a high both early and late mortality. Independent pre-operative risk factors for the development of BCIS were

high ASA scores, COPD, and medication with diuretics and warfarin.

Authors' contributions

All authors gave final approval of the submitted version. F.O.: collected and analysed data and wrote up the first draft; M.K.: collected and analysed data and wrote up the first draft; E.H.: planned and designed the study and interpreted data and revised the manuscript; S.-E.R.: planned and designed the study and interpreted data and revised the manuscript.

Declaration of interest

None declared.

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