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Are AHA/ACC and ESC/ESA Guidelines for Cardiovascular Assessment in Non-Cardiac Surgery Suitable for Fragility Fracture Patients?

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Abstract

In Italy more than 90,000 patients are admitted every year for surgical treatment of hip fracture. In these elderly patients frailty and the presence of 2 or more comorbidities are associated with a prognosis both a 30 days and at 1 year. Heart failure and myocardial infarction are the more threatened cardiac complications and the more frequent causes of death in first 30 days after surgery for hip fracture. High risk patients may be identified by careful and rapid preoperative evaluation in order to decrease preventable in-hospital death in subjects patients candidate to narrow time-dependent surgery. In our review we tried to evaluate whether the ACC/AHA and ESC/ESA guideline are effectively suitable for adequate cardiovascular assessment in this particular high risk population.

Kyewords: Non-cardiac surgery; Fragility fracture; Comorbidity; AHA/ACC guideline; ESC/ESA guideline

Short Communication

In developed countries fragility fractures, and in particular fractures of third proximal of femur, is one of the more frequent causes of admission to emergency department [1]. Only in Italy 90,000 patients are admitted every year for surgical treatment of hip fracture [1,2]. Mean age of these patients is 85 years and a history of cardiovascular disease is found in more than 30% [3]. Moreover at least 50% of these patients have severe functional impairment, with inability to cover more than 50 meters without help, before trauma. Surgery performed within 48 hours from trauma has been demonstrated to significantly improve 30 day and 1 year survival [4-6]. However, these results may be biased by the delay needed for stabilization in patients with more severe clinical conditions at admission. Heart failure and perioperative myocardial infarction are the more threatened cardiac complications and the more frequent causes of death in first 30 days after hip fracture surgery [7]. Severe transient hypotension may occur as a consequence of surgical bleeding and decrease of systemic vascular resistance due to spinal anesthesia. A significant decrease of cardiac output may lead to ominous consequences in patients with severe aortic stenosis and/or severe coronary artery disease.

Rapid and careful preoperative assessment allows identifying high risk patients and decreasing preventable in-hospital deaths in candidates to narrow time-dependent surgery. The choice of proper anesthesiology strategy and perioperative treatment, including postoperative observation in ICU when needed, may improve in hospital survival. The introduction of geriatricians in orthopedic wards and thereafter of orthogeriatrics teams with a multidisciplinary approach has significantly improved in hospital and long term outcomes in patients with hip fracture [8-10]. In Florence exists since 2011 a multidisciplinary team including internal medicine specialists, geriatrics, orthopedics, anesthesiologists that may contribute, through careful clinical evaluation to safely decrease time to surgery, decrease post-operative complications and the length of hospitalization [11]. Are in this setting ACC/AHA and ESC/ESA guidelines effectively suitable for adequate cardiovascular assessment? [12,13]. The first aspect to be discussed is whether hip fracture surgery should be considered a surgical procedure at intermediate risk as reported in the guidelines? The hospital mortality in patients undergoing hip surgery fracture ranges between 2.5 and 9% while 1 years survival is comprised between 65 to 75% [14-17]. In our opinion therefore the frail population undergoing hip fracture surgery should be considered as a high risk group undergoing high risk surgery.

Determination of functional capacity is considered a main step in preoperative cardiac risk assessment for non-cardiac surgery in AHA/ACC or ESC/ESA guidelines: Patients with high functional capacity have been demonstrated to have a good prognosis after non-cardiac surgery also in presence of stable coronary artery disease. Limited activity before trauma may mask symptoms, in particular chest pain and dyspnea, even in presence of history of heart disease. Since most has a poor functional capacity before trauma (largely 4 METs) we cannot rely on this feature for assessment of cardiovascular risk in patients with hip fracture.

In patients undergoing hip fracture surgery the overall rate of postoperative heart failure is close to 7% within seven postoperative days and 22% within one postoperative year. Postoperative heart failure was significantly more common among those with preoperative heart failure and coronary heart disease. In these patients one year mortality was 37% [18]. In a prospective observational study factors related to post-operative heart failure were age ≥ 90 years (OR 4.1), male gender (OR 1.8), and a history of cardiovascular disease (OR 2.3) [19].

The risk of heart failure or death in post-operative period is significantly increased in patients with previously undiagnosed severe valve heart disease, mainly aortic stenosis and mitral regurgitation. According to ESC guidelines routine rest echocardiography may be considered (evidence class II, level B) for the evaluation high-risk surgery patients while recommendation class I evidence level A has been provided for patients with heart failure and recommendation class I evidence level C for patients with physical signs of severe valve disease. According to SIGN guidelines echocardiography is recommended in order to better stratify surgical risk and define anesthesiologist strategy

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in suspected aortic stenosis, provided that examination do not delay surgery [20].

Several information may be provided by echocardiography useful both to obtain more accurate risk stratification and to stabilize clinical conditions. First evaluation of inferior vena cava diameter may allow assessing volume status and correcting before surgery conditions of hypovolemia, which affects adversely clinical outcome. The functional evaluation of left and right ventricle is useful to avoid unnecessary fluid administration which may precipitate heart failure in particular in post-operative period. In patients with suspect heart valve disease, assessment of hemodynamic severity of defects may favor a more accurate peri-operative management. Finally other parameters, in particular pulmonary artery pressure, may provide prognostic elements. According to data from our center in patients with mild-moderate heart failure a RV/RA gradient>40 mmHg is independently associated with a lower in hospital and 3 months survival. We believe that in patients with hip fracture echocardiography performed at admission may give several anatomic and functional parameters, for example inferior vena cava diameter to assess volume status, that may improve peri-operative management and decrease in hospital complications. Further studies must be addressed to evaluate cost-effectiveness in hip fracture units in which bed-side echocardiography may available routinely.

A evidence class II, level B is attributed to NT-pro-BNP and BNP measurements for obtaining independent prognostic information for perioperative and late cardiac events in high-risk patients. A few reports suggest the usefulness of NT-pro-BNP levels as prognostic factor hip fracture surgery [21,22]. In 75 patients with mild moderate heart failure referred to our Hospital for hip fracture NT-pro-BNP values 2000 pg/ml, were associated with a two folds increase in 3 months mortality (64% sensitivity and 70% specificity) [23].

Perioperative myocardial infarction rarely complicates clinical course in patients with hip fracture, however clinical symptoms are uncommon. Patients with perioperative myocardial infarction have a higher 30 days and 1-year mortality. ESC guidelines suggest assessment of cardiac troponins in high-risk patients, both before and 48-72 hours after major surgery, may be considered (evidence class II level b). According to the diagnostic criteria used in different studies the incidence of perioperative acute myocardial infarction in patients hospitalized for hip fracture varies from 6%-35% [24-26].

A retrospective study from Olmsted County, Minnesota reported among 1212 consecutive patients admitted for hip fracture a 13.8% incidence of perioperative myocardial infarction, most occurring in the first 48 hours after surgery [27]. In-hospital mortality was 14.4% while 1-year survival was 60.5%. The authors conclude that the majority of patients did not experience ischemic symptoms and required cardiac biomarkers for the diagnosis.

Hietala observed an increase of TnT in 35.5% in hip fracture surgery [28]. Near half of these patients showed troponin increase before surgery. Overall 30-day mortality was 17% and 24% in subgroup with values 0.15 μg/L. In this study increase of troponin was the only independent predictor of 30-day mortality. Fisher showed that a perioperative increase of troponin I 0.06 μg/L was associated with longer hospitalization and referral to long term residential care facilities. A troponin I 1 μg/L was predictor of all-cause mortality with 98% specificity and 89% negative predictive value.

Perioperative myocardial infarction has been often the first clinical manifestation of coronary heart disease. 56% of patients referred for surgical treatment of hip fracture that showed an increase of troponin levels had no previous history of coronary artery disease.

The finding that a significant troponin increase is found before surgery in 20-40% of perioperative myocardial infarctions suggests that troponin assay should be performed at hospital admission [28]. In patients with elevated TnI at admission clinical stabilization may be needed before surgery. In our experience time to surgery was longer in patients with elevated preoperative TnI (4.4 days) compared with those with normal TnI value at admission (2.5 days).

Nevertheless hospital and long-term mortality were lower, although not statistically significant, in patients with preoperative elevated TnI than in patients with postoperative myocardial infarction [29].

At present no indication is provided by ESC/ESA or AHA/ACC guidelines for early invasive evaluation in subjects suffering from perioperative myocardial infarction after non-cardiac surgery and to our knowledge the effects of early revascularization have not been previously studied in these patients In our institution 13/99 patients with peri-operative myocardial infarction underwent coronary angiography and subsequent revascularization after hip surgery, 12 percutaneous and 1 surgical (associated with mitral valve repair for severe mitral valve regurgitation). Eleven (82%) were alive at 1 year of follow-up in comparison to 38/88 (42%) patients treated with medical therapy.

An emergent issue in preoperative evaluationof hip fracture patients is the growing number (about 20%) with on going anticoagulant (warfarin or direct oral anticoagulants) or double antiplatelet treatment.

Bleeding risk is increased in these during non-cardiac surgery; however this risk will be outweighed by the benefit of anticoagulant-antiplatelet therapy. Since hip fracture treatment is a close time dependent surgery restoration of coagulative activity is usually a primary need for anesthesiologists and surgeons. The topic is not clearly addressed by guidelines. Anticoagulant doses of LMWH (bridge therapy) have been suggested in high risk patients (mechanical valve in mitral position, previous stroke or TIA, recent venous thromboembolism) [30], however an increase of bleeding complications of has been provided for "full doses" of LMWH [31]. LMWH at dosage used for DVT prophylaxis is safe in most patients without a higher thromboembolic risk and a decrease of hemorrhagic complications. Reversal of warfarin effects with vitamin K administration may significantly shorten the time to surgery in anti-coagulated patients. Limited evidence exists on effects of low-dose vitamin K administration before hip surgery, suggesting a decrease in time to surgery without an increased embolic risk.

Surgery should be delayed 48-72 hours in in patients treated with direct anticoagulant agents at the moment of trauma. Few data were published about the impact of oral anticoagulation on time to surgery in patients hospitalized with hip fracture. Tran et al. reported that patients in DOAC had a longer time to surgery (66.9 h; IQR: 38.1 to 78.9) compared to a to the control group (26.2 h; IQR: 17.3 to 40.6; p b 0.0001) [32].

Similarly in our experience in 31 patients in DOA treatment time to surgery was 4.0 ± 2.58 days *vs.* 2.65 ± 1.64 days in control group. We did not find significant differences in hospital mortality between two groups (3.9% in DOA patients in comparison to 3% in controls).

Prothrombin complex concentrates activated prothrombin complex concentrates (FEIBA) may contribute to "reverse" anticoagulation

induced by Xa factor inhibitors in order to decrease the time to surgery however no data exist in patients with hip fracture [33,34].

Recently REVERSE- AD study, evaluated the effects of Idarucizumab i.v (5 mg) in reversing dabigatran effects. Were enrolled two groups: Group A (patients who had uncontrolled bleeding) and Group B (patients who needed an urgent surgical or interventional procedure) [35]. In this second group 20% of patients had hip fracture. The study showed that the surgical/interventional procedure was started on average 1.6 hours after Idarucizumab administration with normalization of hemostasis in 93.4% before starting the procedure.

The authors did not show provide data isolated data for hip fracture surgery. Further studies are needed to further assess the cost-effectiveness of this approach.

The risks associated with the operative management of patients on double antiplatelet agents include increased intra-operative bleeding and a higher risk of spinal haematoma where regional anaesthesia is used. In patients needing surgery within a few days, current ESC Guidelines recommend withholding clopidogrel and ticagrelor for five days and prasugrel for seven days prior to surgery unless there is a high thrombotic risk.

Withdrawal of antiplatelet agents and waiting reverse of pharmacological effects before surgery is associated with an unacceptable delay in surgery (8 *vs.* 2 days) and significant increase in the risk of perioperative stent thrombosis, overall hospital complications, and mortality [36]. Hip surgery has been performed safely under general anaesthesia in patients with ongoing double antiplatelet treatment for recent coronary stenting without a significant increase in morbidity and mortality. However they showed an increase in the need for blood transfusions [37-39].

Rarely platelet transfusion may be needed for uncontrollable bleeding. Simple validated score systems may be useful to stratify surgical risk in analogy with cardiac surgery. In the risk calculator score proposed by Pugely et al. risk variables were variables American Society of Anesthesia score, dependence in BADL, active malignancy, race, cardiopulmonary disease, renal failure, longer surgical time and open versus percutaneous surgery [40]. A new prognostic score index, is presently under validation at our institution.

In conclusion ACC/AHA and ESC guidelines have several limitations for the assessment of cardiovascular risk in patients who need time dependent surgery as needed for hip fracture. A careful clinical preoperative evaluation including echocardiography may favor to decrease the risk of severe complications and preventable deaths.

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