

Atrial Fibrillation in Patients Undergoing Hip Fracture Surgery

Carlo Rostagno MD, PhD

Carlo Rostagno, Department of Experimental and Clinical Medicine, University of Florence, Italy

Conflict-of-interest statement: The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Carlo Rostagno, Department of Experimental and Clinical Medicine, University of Florence, Italy.

Email: carlo.rostagno@unifi.it

Telephone: +390557948545

Fax: +390558547

Received: May 28, 2018

Revised: July 30, 2018

Accepted: August 1 2018

Published online: February 2, 2019

ABSTRACT

More than 90% of hip fracture patients are older than 70 years and in most studies mean age is close to 85 years. Increasing age is also associated with a higher prevalence of atrial fibrillation (AF). In present review we will try to answer 3 main questions about the effect of atrial fibrillation in patients with hip fracture: (a) Is there a relationship between AF and risk of hip fracture? (b) Which should be perioperative management of anticoagulant treatment? (c) Has AF a long term prognostic value on survival after hip fracture surgery and is there a relationship between AF and the results of rehabilitative treatment? Moreover we evaluated the few reports about incidence and prognostic value of new onset postoperative atrial fibrillation.

Key words: Atrial fibrillation; Hip fracture; Anticoagulant treatment; Prognosis

© 2019 The Author(s). Published by ACT Publishing Group Ltd. All rights reserved.

Rostagno C. Atrial Fibrillation in Patients Undergoing Hip Fracture Surgery. *Journal of Cardiology and Therapy* 2019; **6(1)**: 764-767 Available from: URL: <http://www.ghrnet.org/index.php/jct/article/view/2352>

INTRODUCTION

Fragility fractures are responsible for 300,000 annual UK emergency department attendances and over 9 million annual fractures worldwide^[1,2]. In Italy every year approximately 90,000 patients undergo surgery for hip fracture^[3]. More than 90% of hip fracture patients are older than 70 years and in most studies mean age is close to 85 years^[4,5]. Increasing age is associated with a higher prevalence of atrial fibrillation (AF)^[6]. Between 12 and 14% of patients admitted to our institution for hip fracture were in atrial fibrillation before surgery. Moreover patients in sinus rhythm at admission, due to age and comorbidities, are at an increased risk of developing postoperative atrial fibrillation (POAF)^[7]. Aim of this review was to evaluate the effects of both preexistent and postoperative atrial fibrillation in patients undergoing hip fracture surgery.

PREEXISTING ATRIAL FIBRILLATION

The incidence of atrial fibrillation at admission in patients referred to hospital for hip fracture has been reported between 7 and 10%^[8,9] but is probably underestimated. In a case control study including 888 patients (444 cases), after correction for potential confounders, atrial fibrillation was the more frequent ECG abnormality associated with hip fractures (OR 2.7; 95% CI 1.2-6.1)^[10].

In present review we will try to answer 3 main questions about the effect of preexisting atrial fibrillation and hip fracture: (a) Is there a relationship between AF and risk of hip fracture? (b) Which should be perioperative management of anticoagulant treatment? (c) Has AF a long term prognostic value on survival after hip fracture surgery and is there a relationship between AF and the results of rehabilitative treatment?

Regarding the first question a number of cardiovascular diseases have been related to an increased risk of osteoporotic fracture. At present limited information is available in literature about the relation between atrial fibrillation (AF) and subsequent fragility fracture risk.

In the study by Wong et al^[11] clinical and hospitalization information of 113,600 individuals were linked over a 14-year period, Annualized incidence of hip fracture was 17.5 per 1000 person-years (95% CI 16.8-18.1) in those with AF in comparison to 7.4 per 1000 person-years (95% CI 7.1-7.7) in those without AF. Unadjusted risk ratio for patients with AF was 2.39 (95% CI 1.96-2.91) in men and 2.91 (95% CI 2.55-3.34) in women. After adjusting for potential confounders, these associations were attenuated but remained statistically significant. Conversely an association of incident AF with the risk of subsequent falls or hip or other fractures was not shown in the Cardiovascular Health Study (CHS) cohort^[12]. Individuals with AF were not found to have a higher risk of hip fracture (adjusted HR = 1.09, 95 % CI 0.83-1.42) or fracture at any selected site (adjusted HR = 0.97, 95 % CI 0.77-1.22) compared with those without AF.

Although at present data are contrasting, patients with a history of AF may represent a clinical population in whom screening for and treatment of osteoporosis may be warranted to reduce the risk of subsequent fracture.

Perioperative management of anticoagulant treatment is a relevant factor in fragility fractures patients. At least 20% of patients with hip fracture are on ongoing anticoagulant (both warfarin and direct oral anticoagulants) at the moment of hospitalization. Since hip fracture treatment is a close time-dependent surgery, restoration of coagulative activity is usually a primary need for anesthesiologists and surgeons. Bridge therapy with LMWH at anticoagulant dose may be considered for high risk patients (mechanical valve in mitral position, previous stroke or TIA, recent venous thromboembolism)^[13] but the matter is still debated and recent data suggested an increased risk of postoperative bleeding in patients treated with “full doses” of LMWH^[14]. LMWH at dosage used for DVT prophylaxis is safe in most patients without an increased risk of thromboembolism and with a lower risk of hemorrhagic complications.

Another problem in high risk patients may be the safety of rapid correction of anticoagulation with vitamin K administration. At present few data have published about the balance between an increased risk of embolism and the advantage of early hip surgery. Moores et al^[15] reported that a low intravenous dose of vitamin K (mean of 2.2 -range, 0-4- administrations of 2 mg of vitamin K.) allowed to decrease mean INR from 2.6 (range, 1.1-4.6) to < 1.7 within 18 hours (mean, 14 hours). 78% of patients underwent surgery within 36 hours in 46 low risk patients in warfarin therapy. The 3 high-risk patients (prosthetic heart valve) underwent bridging therapy with low-molecular-weight heparin and received no vitamin K; their mean INR on admission was 3.2 (range, 3.1-3.3) and the mean time to surgery was 5.3 (range, 3-8) days. Two low-risk patients and one high-risk patient died within 5 days of surgery. Overall 30-day and one-year mortality were 8.2% and 32.6%, respectively.

Data from our Institution suggest that vitamin K administered per os (10 mg eventually repeated after 24 hours) is associated with a lower time to surgery and a trend to lower in hospital mortality. Moreover patients not treated with vitamin K had a higher incidence of deep venous thrombosis despite LMWH prophylaxis, likely due to longer time to surgery.

Surgery should be delayed 48-72 hours in patients in treatment with direct anticoagulant agents at the moment of trauma, however limited data exist about the impact of oral anticoagulation on time to surgery in patients hospitalized with hip fracture. Tran et al^[16] reported that patients in DOAC had a longer time to surgery compared to a to the control group (66.9 h; range 38.1 to 78.9 vs 26.2 h; range: 17.3 to 40.6; $p < 0.0001$). 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).

No data are reported in patients with hip fracture on the role of prothrombin complex concentrates and activated prothrombin complex concentrates (FEIBA) to “reverse” anticoagulation induced by Xa factor inhibitors in order to decrease time to surgery.

Recently the REVERSE- AD study^[17] evaluated the effects of 5 g of intravenous idarucizumab in reversing the anticoagulant effect of dabigatran in patients. The study included two groups: the first who had uncontrolled bleeding (group A) the second who needed an urgent procedure (group B). In this second group 20% of patients had hip fracture. In group B median time to beginning of intended procedure was 1.6 hours and peri-procedural hemostasis was assessed as normal in 93.4% of the patients. The authors however did not gave separate results for patients with hip fracture. Further studies are needed to assess the cost-effectiveness of this approach.

3 Despite the high incidence of atrial fibrillation in patients with fragility fractures limited data exist about its relation with in hospital and long-term prognosis after surgery. Adunski et al^[18] evaluated long term prognostic value of AF in hip fracture patients. 1114 consecutive patients were divided into three groups: patients with sinus rhythm (SR), paroxysmal atrial fibrillation (PAF) or chronic atrial fibrillation (CAF). Patients with AF were older, had a more frequent history of heart failure, ischemic heart disease and stroke. Patients with permanent AF (but not PAF or SR) had a higher risk of death at both 365 days and at the end of the study (HR 1.786, CI 1.011- 3.155 and HR 1.835, CI 1.302-2.585, respectively). Older age and male gender also predicted higher risk of death at both 365 days and at the end of the study. However AF, in the same group, was not associated with rehabilitation outcome of these patients^[19], it was mainly related to motor Functional Independence Measure scores at discharge and postfracture changes in functional status. In 792 consecutive patients underwent hip fracture surgery at our Institution AF was independently associated with in hospital mortality (OR = 5.8, 95% CI 3.5-12.2).

Male gender and renal failure were also associated with higher mortality while functional status before trauma was associated with a higher survival rate. Nevertheless we did not find significant difference in survival at 1 year follow-up between patients with or without atrial fibrillation at the moment of surgery.

POST-OPERATIVE ATRIAL FIBRILLATION

Until recently post-operative atrial fibrillation (POAF) after non cardiac surgery it was considered a self-limited entity with a quite favorable long-term prognosis. However knowledge of POAF largely relies on retrospective studies and analysis of administrative datasets. Moreover at present there are no high quality prospective studies to direct clinical management of these patients. An increased sympathetic tone, related to pain, anemia, hypoxia, hypoglycemia, hyperthyroidism, changes in volume status and hypotension, or to surgery itself, is considered the main trigger for POAF^[20]. Administration of perioperative catecholamine may sometimes favor POAF. Changes in cellular resting potentials, automaticity, and excitability due to electrolyte abnormalities, in particular hypokalemia, is also associated with an increased risk of POAF^[21]. Myocardial ischemia may contribute to POAF in hip fracture surgery. Recently high sensitive troponin I ≥ 6.5 ng/L was reported to be associated with a 5 fold risk increase of POAF (17.8 vs 3.2%)^[22].

The incidence of POAF in non-cardiothoracic surgery is lower than in cardiothoracic surgery and ranges from 12%-19% for abdominal surgery to 4.8% after total joint replacements^[7,23-25]. After NCTS, patients usually return in a general ward without continuous cardiac monitoring. Diagnosis is made usually at symptoms onset or eventually during clinical reevaluation. Therefore exact timing of onset of POAF is unclear and asymptomatic episodes may never be detected. No clear indication exists about treatment of arrhythmia, amiodarone being the most used drug, nor about the need for subsequent anticoagulation. POAF in non-cardiac non-thoracic surgery is associated with significant morbidity and mortality and an increase in resource utilization, length of stay, re hospitalization and finally with an increased risk of stroke. Since long-term follow-up data are limited and AF may recur, these patients should receive careful reassessment and follow-up. In patients who recover rapidly sinus rhythm careful monitoring it is difficult to justify long-term anticoagulation unless recurrent episodes of AF are documented.

Limited data address the significance of perioperative atrial fibrillation (AF) and its subsequent treatment in emergent orthopedic surgery in the elderly. Leibowitz et al^[26] retrospectively studied the outcome of newly diagnosed AF among patients initially in sinus rhythm undergoing hip fracture repair. In 410 subjects over the age of 65 who underwent repair of hip fracture 15 (3.7%) developed AF during hospitalization. Only a previous history of AF and current use of beta blockers were predictive of the development of AF following hip surgery. Mortality among patients with new onset AF was significantly higher than in patients without AF (60% vs 19.5%; $p < 0.001$). Chronic treatment with anti-arrhythmic therapy as well as treatment with anticoagulation was also associated with one-year mortality. On multivariable analysis, AF during hospitalization was the variable most significantly associated with mortality (hazard ratio 6.7 95% CI 2.1-21.4). Between February 2012 and July 2016 3129 patients were referred to trauma Center of AOU Careggi (Florence). Two hundred and seventy seven were in permanent atrial fibrillation at hospital admission and were excluded from the study. Overall 104 patients (mean age 84 years, females 73%) developed a POAF (3.4%). Average time of onset after surgery was 2 days. Eight patients died during hospitalization. 81.7% were discharged in sinus rhythm. POAF group in comparison to control group (e.g patients in stable sinus rhythm) had a longer time to surgery (2.4 ± 1.6 days vs 3.8 ± 3.3 days) and length in hospital stay (14.4 ± 5.1 days vs 19.7 ± 10.4 days). Furthermore 1-year mortality was significantly higher in POAF group in comparison to control group (39.3% vs 20.9%, $p < 0.001$).

At present we have no clearly demonstrated risk factors for POAF. An history of paroxysmal AF, the presence of at least moderate mitral regurgitation and increased preoperative high sensitive troponin I may be related with an higher probability of developing POAF. As well there are no suggested treatment strategies both for rhythm recovery and for long term anticoagulation. The growing collaboration between orthopedics and clinicians may help to find an answer.

REFERENCES

1. Kanis JA, Oden A, Johnell O, Jonsson B, de Laet C, Dawson A. The burden of osteoporotic fractures: a method for setting intervention thresholds. *Osteoporos Int* 2001; **12**: 417-427. [PMID: 11444092]; [DOI: 10.1007/s001980170112]
2. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporos Int* 2006; **17**: 1726-1733. [PMID: 16983459]; [DOI: 10.1007/s00198-006-0172-4]
3. Piscitelli P, Brandi ML, Chitano G, Argentiero A, Neglia C, Distante A, Saturnino L, Tarantino U. Epidemiology of fragility fractures in Italy. *Clin Cases Miner Bone Metab*. 2011 May; **8**(2): 29-34. [PMID: 22461813]; [PMCID: PMC3279081]
4. Veronese N, Maggi S. Epidemiology and social costs of hip fracture. *Injury*. 2018 Aug; **49**(8): 1458-1460. [PMID: 29699731]; [DOI: 10.1016/j.injury.2018.04.015]
5. Rapp K, Büchele G, Dreinhöfer K, Bücking B, Becker C, Benzinger P. Epidemiology of hip fractures: Systematic literature review of German data and an overview of the international literature. *Z Gerontol Geriatr*. 2018 Mar 28. [PMID: 29594444]; [DOI: 10.1007/s00391-018-1382-z]
6. Ohlmeier C, Mikolajczyk R, Haverkamp W, Garbe E. Incidence, prevalence, and antithrombotic management of atrial fibrillation in elderly Germans. *Europace*. 2013; **15**: 1436-1444. [PMID: 23487542]; [DOI: 10.1093/europace/eut048]
7. Bessissow A, Khan J, Devereaux PJ, Alvarez-Garcia J, Alonso-Coello P. Postoperative atrial fibrillation in non-cardiac and cardiac surgery: an overview. *J Thromb Haemost*. 2015 Jun; **13** Suppl 1: S304-12. [PMID: 26149040]; [DOI: 10.1111/jth.12974]
8. Kim BH, Lee S, Yoo B, Lee WY, Lim Y, Kim MC, Yon JH, Kim KM. Risk factors associated with outcomes of hip fracture surgery in elderly patients. *Korean J Anesthesiol*. 2015 Dec; **68**(6): 561-7. [PMID: 26634079]; [PMCID: PMC4667141]; [DOI: 10.4097/kjae.2015.68.6.561]
9. Kilci O, Un C, Sacan O, Gamli M, Baskan S, Baydar M, Ozkurt B. Postoperative Mortality after Hip Fracture Surgery: A 3 Years Follow Up. *PLoS One*. 2016 Oct 27; **11**(10): e0162097. [PMID: 27788137]; [PMCID: PMC5082940]; [DOI: 10.1371/journal.pone.0162097]
10. Jansen S, Koster RW, de Lange FJ, Goslings JC, Schafroth MU, de Rooij SE, van der Velde N. Electrocardiographic abnormalities in patients admitted for hip fracture. *Neth J Med*. 2014 Nov; **72**(9): 455-61. [PMID: 25431390]
11. Wong CX, Gan SW, Lee SW, et al Atrial fibrillation and risk of hip fracture: A population-based analysis of 113,600 individuals. *Int J Cardiol* 2017 Sep 15; **243**: 229-232. [PMID: 28528985]; [DOI: 10.1016/j.ijcard.2017.05.012]
12. Wallace ER, Siscovick DS, Sitlani CM, Dublin S, Mitchell P, Robbins JA, Fink HA, Cauley JA, Bůžková P, Carbone L, Chen Z, Heckbert SR. Incident atrial fibrillation and the risk of fracture in the cardiovascular health study. *Osteoporos Int*. 2017 Feb; **28**(2): 719-725. [PMID: 27714443]; [PMCID: PMC5782802]; [DOI: 10.1007/s00198-016-3778-1]
13. Douketis JD, Spyropoulos AC, Spencer FA, Mayr M, Jaffer AK, Eckman MH, Dunn AS, Kunz R. Perioperative management of antithrombotic therapy: Antithrombotic therapy and prevention of thrombosis, 9th ed: American college of chest physicians evidence-based clinical practice guidelines. *Chest* 2012; **141**: e326S-e350S. [PMID: 22315266]; [PMCID: PMC3278059]; [DOI: 10.1378/chest.11-2298]
14. Douketis JD, Spyropoulos AC, Kaatz S. Perioperative bridging anticoagulation in patients with atrial fibrillation. *N Engl J Med* 2015; **373**: 823-833.
15. Moores TS, Beaven A, Cattell AE, Baker C, Roberts PJ. Preoperative warfarin reversal for early hip fracture surgery. *J Orthop Surg (Hong Kong)*. 2015 Apr; **23**(1): 33-6. [PMID: 25920640]; [DOI: 10.1177/230949901502300108]
16. Tran T, Delluc A, de Wit C, Petreich W, Le Gal G, Carrier M. The impact of oral anticoagulation on time to surgery in patients hospitalized with hip fracture. *Thromb Res* 2015; **136**: 962-965. [PMID: 26428416]; [DOI: 10.1016/j.thromres.2015.09.017]
17. Pollack CV, Reilly PA, Van Ryn J. Idarucizumab for dabigatran reversal full cohort analysis. *N Engl J Med* 2017; **377**: 431-441. [PMID: 28693366]; [DOI: 10.1056/NEJMoa1707278]
18. Adunski Arad M, Koren-Morag N, Fleissig Y, Mizrahi

- EH. Increased 1-year mortality rates among elderly hip fracture patients with atrial fibrillation. *Aging Clin Exp Res*. 2012 Jun; **24**(3): 233-8. [PMID: 23114549]
19. Adunsky A, Arad M, Koren-Morag N, Fleissig Y, Mizrahi EH. Atrial fibrillation is not associated with rehabilitation outcomes of elderly hip fracture patients. *Geriatr Gerontol Int*. 2012 Oct; **12**(4): 688-94. [DOI: 10.1111/j.1447-0594.2012.00845.x]
 20. Heintz KM, Hollenberg SM. Perioperative cardiac issues: postoperative arrhythmias. *The Surgical clinics of North America*. 2005; **85**: 1103-14. [PMID: 16326196]; [DOI: 10.1016/j.suc.2005.09.003]
 21. Chelazzi C, Villa G, De Gaudio AR. Postoperative atrial fibrillation. *ISRN cardiology*. 2011; **2011**: 203179. [PMID: 22347631]; [PMCID: PMC3262508]; [DOI: 10.5402/2011/203179]
 22. Kim BS, Kim TH, Oh JH, Kwon CH, Kim SH, Kim HJ, Hwang HK, Chung SM. Association between preoperative high sensitive troponin I levels and cardiovascular events after hip fracture surgery in the elderly. *J Geriatr Cardiol*. 2018 Mar; **15**(3): 215-221. [PMID: 29721000]; [PMCID: PMC5919809]; [DOI: 10.11909/j.issn.1671-5411.2018.03.002]
 23. Walsh SR, Tang T, Wijewardena C, Yarham SI, Boyle JR, Gaunt ME. Postoperative arrhythmias in general surgical patients. *Annals of the Royal College of Surgeons of England*. 2007; **89**: 91-5. [PMID: 17346395]; [PMCID: PMC1964549]; [DOI: 10.1308/003588407X168253]
 24. Christians KK, Wu B, Quebbeman EJ, Brasel KJ. Postoperative atrial fibrillation in non cardiothoracic surgical patients. *American journal of surgery*. 2001; **182**: 713-5. [PMID: 11839344]
 25. Kahn RL, Hargett MJ, Urquhart B, Sharrock NE, Peterson MG.. Supraventricular tachyarrhythmias during total joint arthroplasty. Incidence and risk. *Clinical orthopaedics and related research*. 1993 Nov; **296**: 265-9. [PMID: 8222436]
 26. Leibowitz D, Abitbol C, Alcalai R, Rivkin G, Kandel L. Perioperative atrial fibrillation is associated with increased one-year mortality in elderly patients after repair of hip fracture. *Int J Cardiol*. 2017 Jan 15; **227**: 58-60. [DOI: 10.1016/j.ijcard.2016.11.067. Epub 2016 Nov 9]