Overweight and Aging Increase the Risk of Atrial Fibrillation After Cardiac Surgery Independently of Left Atrial Size and Left Ventricular Ejection Fraction

Pier Luigi Stefano
  Department of Cardiothoracovascular Medicine, Careggi University Hospital, Florence

Marco Bugetti
  Department of Cardiothoracovascular Medicine, Careggi University Hospital, Florence

Guido Del Monaco
  Department of Cardiothoracovascular Medicine, Careggi University Hospital, Florence

Gloria Popescu
  Department of Cardiothoracovascular Medicine, Careggi University Hospital, Florence

Paolo Pieragnoli
  Department of Cardiothoracovascular Medicine, Careggi University Hospital, Florence

Giuseppe Ricciardi
  Department of Cardiothoracovascular Medicine, Careggi University Hospital, Florence

Laura Perrotta
  Department of Cardiothoracovascular Medicine, Careggi University Hospital, Florence

Luca Checchi
  Department of Cardiothoracovascular Medicine, Careggi University Hospital, Florence

Roberto Rondine
  Department of Cardiothoracovascular Medicine, Careggi University Hospital, Florence

Sergio Bevilacqua
  Department of Cardiothoracovascular Medicine, Careggi University Hospital, Florence

Niccolò Marchionni
  Department of Cardiothoracovascular Medicine, Careggi University Hospital, Florence

Antonio Michelucci (antonio.michelucci@unifi.it)
  University of Florence  https://orcid.org/0000-0002-4661-4193

Research article

Keywords: postoperative atrial fibrillation, cardiac surgery, risk factors.

DOI: https://doi.org/10.21203/rs.3.rs-49937/v1
Abstract

**Background:** Body mass index (BMI), age, left atrium (LA) dimensions and left ventricular ejection fraction (LVEF) have been linked to post-operative atrial fibrillation (POAF) after cardiac surgery. The aim was to better define the role of these risk factors.

**Methods:** This study evaluated 249 patients (without prior atrial dysrhythmia) undergoing cardiac or aortic surgery. Prior to surgery the following data were collected: age (yrs), BMI (kg/m2), LA diameter (cm), LA area (cm2), LVEF (%), the presence of arterial hypertension (AH) and of diabetes, thyroid stimulating hormone (TSH, mU/L) and, creatinine (mg/dL).

**Results:** Patients with (n. 127, 51%) and without POAF (n. 122, 49%) were compared. No difference was observed for sex, LA diameter, LA area, LVEF, TSH and diabetes. Instead, patients with PoAF had higher values of age, BMI, creatinine and a greater prevalence of AH and Bentall procedures. Multivariable analysis showed that the only independent predictors of PoAF were: age (OR = 1,05, CI 95% 1,025-1,076, p= 0,0001) and BMI (OR=1,095, CI 95% 1,015-1,182, p= 0,019).

**Conclusions:** Results suggest that advanced age and a higher value of BMI are strong risk factors for POAF in patients without previous AF. This even in the presence of comparable LA dimensions and LVEF.

1. **Introduction**

Because of persistent high incidence, increased complications, length of hospitalization and costs, post-operative atrial fibrillation (POAF) is still a major problem in cardiac surgery [1–4]. It is therefore useful to determine which clinical and instrumental factors identify patients at increased risk of developing POAF.

A close association has been reported between obesity and atrial fibrillation [5]. However, almost all studies reporting such association have used the Body Mass Index (BMI, Kg/m^2^) to evaluate weight excess [6]. Indeed, BMI is still considered the most practical parameter taken to represent the role played by overweight [7], while other recognized risk factors for POAF are advanced age [8, 9], left atrial dimension [10, 11] and left ventricular systolic dysfunction [12, 13].

The aim of the present study was to better define the relative role played by these risk factors comparing patients with and without POAF. To eliminate the arrhythmia itself as a confounder, only patients without a previous history of atrial fibrillation were included in the study.

2. **Methods:**

2.1. **Study population and data collection**

This study included 249 consecutive patients (mean age 65.6 ± 14.7, range 19-90 years, M/F 156/93) who during year 2019 underwent cardiac or aortic surgery in a tertiary hospital in Florence, Italy. Patients
undergoing emergency surgery, and those with prior atrial dysrhythmia (based on clinical history and review of medical records), were excluded. The following data were systematically collected 24 hours before surgery: age (yrs), BMI, left atrium (LA) diameter (cm), LA area (cm²), left ventricular ejection fraction (LVEF, %), the presence/absence of arterial hypertension (AH) and diabetes, and creatinine (mg/dL). To detect the occurrence of incident POAF, cardiac rhythm was continuously recorded during the first seven postoperative days. The end-point of the study was the occurrence of POAF during the early postoperative period (i.e. the time between surgery and discharge, defined as any sustained (i.e. >10 min) recorded episodes [6,8]. Antiarrhythmic agents, such as amiodarone, were most frequently used as a treatment option, alone or in combination with electric cardioversion.

This study received approval from the institutional review board of the hospital for accessing the electronic medical records of study subjects, and for collecting and processing relevant data from these records. The research plan was submitted to the department of cardiovascular surgery and nursing departments to report the purpose and method of the study and to obtain permission for data collection. This investigation conformed to the principles outlined in the Declaration of Helsinki.

### 2.2 Statistical analysis

Continuous and categorical variables are presented as mean ± standard deviation or as number and percentage, and were compared with the Student's t-test or the chi-square test, respectively. To identify the independent determinants of incident POAF, we calculated a binary logistic regression model testing the multivariable association of all clinical and instrumental data with POAF, which was considered as the dependent variable. The strength of the association between two variables was expressed as Odds Ratio (OR) and 95% confidence interval (95% CI). All statistical analyses were performed with SPSS V23 package (SPSS Inc., Chicago, IL, USA).

### 3. Results

The main demographic, clinical, laboratory, echocardiographic characteristics, and the surgical procedures of patients without and with (N = 127 51%), incident POAF are reported in Table 1. 
Table 1
Demographic and clinical characteristic in patients without and with incident POAF.

| Variable                           | No  | Yes  | p value |
|------------------------------------|-----|------|---------|
| Age, years (N = 122)               |     |      |         |
| Age, years                         | 60.4 ± 16.4 | 70.6 ± 10.7 | 0.001 |
| Female, n (%)                      | 43 (35.2%) | 50 (39.4%) | 0.501 |
| BMI, kg/m²                         | 24.9 ± 3.6 | 26.8 ± 4.5 | 0.001 |
| Arterial hypertension, n (%)       | 61 (50%)  | 93 (73.2%) | 0.001 |
| Diabetes, n (%)                    | 17 (13.9%) | 23 (18.1%) | 0.370 |
| Creatinine, mg/dL                  | 0.88 ± 0.32 | 1.06 ± 0.91 | 0.038 |
| TSH, mU/L                          | 2.69 ± 4.33 | 1.96 ± 1.69 | 0.133 |
| LA diameter, mm                    | 39.2 ± 8.1 | 40.1 ± 10.1 | 0.702 |
| LA area, cm²                       | 23.9 ± 5.9 | 23.6 ± 5.9 | 0.685 |
| LVEF, %                            | 58.6 ± 9.8 | 57.6 ± 7.9 | 0.411 |
| CABG, n (%)                        | 20 (16.4%) | 31 (24.4%) | 0.117 |
| Mitral valve repair, n (%)         | 31 (25.4%) | 28 (22.0%) | 0.533 |
| Tricuspid valve repair, n (%)      | 10 (8.2%)  | 8 (6.3%)   | 0.563 |
| Aortic valve replacement, n (%)    | 49 (40.2%) | 50 (39.4%) | 0.8982 |
| Mitral valve replacement, n (%)    | 12 (9.8%)  | 9 (7.1%)   | 0.435 |
| Tricuspid valve replacement, n (%) | 1 (0.8%)   | 0          | 0.490 |
| Morrow septal myectomy, n (%)      | 3 (2.5%)   | 5 (3.9%)   | 0.723 |
| Atrial septal defect closure, n (%)| 4 (3.3%)   | 3 (2.4%)   | 0.718 |
| Ascendant aorta replacement, n (%) | 10 (8.2%)  | 9 (7.1%)   | 0.7415 |
| Bentall procedure, n (%)           | 12 (9.8%)  | 31 (24.4%) | 0.02335 |
| Ventricular septal defect closure, n (%) | 2 (1.6%) | 0 | 0.239 |

POAF = Post-operative atrial fibrillation, BMI = body mass index, TSH = thyroid stimulating hormone, LA = Left atrium, LVEF = left ventricular ejection fraction, CABG = Coronary artery bypass graft
Patients with incident POAF were older, had a larger BMI, a greater prevalence of history of arterial hypertension, and a higher baseline creatine. No other laboratory data or echocardiographic parameter, including left atrial dimensions or left ventricular ejection fraction, was significantly different between the two groups. Among the surgical procedures, only the Bentall operation was performed much more frequently in patients with than in those without incident POAF (Table 1).

At multivariable analysis with a binary logistic model that included as covariates all the variables significantly associated with POAF at univariable analysis (age, BMI, arterial hypertension, plasmatic creatinine and Bentall procedure), only age (OR = 1.05, 95%CI 1.025–1.076, p = 0.0001) and BMI (OR = 1.095, 95%CI 1-015-1.182, p = 0.019) were retained as independent predictors of incident POAF.

4. Discussion
Using a real world clinical experience with careful exclusion of patients with a history of atrial tachyarrhythmia, the results of this study highlight in a more convincing way that age and BMI are important POAF risk factors in patients who never had experienced AF prior to surgery. In fact, the association of these two parameters with the probability of incident POAF proved to be independent of left atrial size and ventricular systolic function, and of type of surgery as well.

Advanced age has been defined as one of the most powerful risk factors for incident AF after open heart surgery [8, 9]. This could be interpreted considering the presence of preexisting structural changes of the atria related to ageing and to arterial hypertension.

A BMI beyond the diagnostic threshold of obesity suggests that a low-grade inflammation might be present in patients with POAF [14], and an excess fat, especially epicardial fat, is known to contribute to structural alterations of the atrial tissue [15]. As in previous studies (6,8), we defined POAF as episodes of AF lasting longer than 10 minutes and/or entailing the use of antiarrhythmic therapy or electrical cardioversion. This definition makes it possible to identify the POAF even in the late shipping phase when continuous monitoring is interrupted. The literature suggests that the vast majority of episodes still occur in the first 3–4 days and are generally sustained for more than an hour. Consequently, the risk of unrecognized episodes would be particularly low.

5. Conclusions
The results of this study indicate that age and BMI represent important and independent risk factors for POAF. Moreover, it is important to underline that they play their role regardless of atrial size and ventricular systolic function.

Declarations

Authors' contributions
PLS, NM and AM analyzed, interpreted the patient data and, were the major contributors in writing the manuscript.

References

1. Gudbjartsson T, Helgadottir S, Sigurdsson MI, et al. New-onset postoperative atrial fibrillation after heart surgery. Acta Anaesthesiol Scand. 64(2) (2020) 145–155. doi:10.1111/aas.13507.

2. Arakawa M, Miyata H, Uchida N, et al. Postoperative atrial fibrillation after thoracic aortic surgery. Ann Thorac Surg. 99(1) (2015) 103–108. doi:10.1016/j.athoracsur.2014.08.019.

3. Gorczyca I, Michta K, Pietrzyk E, Woźniakowska-Kaplon B. Predictors of post-operative atrial fibrillation in patients undergoing isolated coronary artery bypass grafting. Kardiol Pol. 76(1) (2018) 195-201. doi: 10.5603/KP.a2017.0203.

4. Pillarisetti J, Patel A, Bommana S, Guda R, Falbe J, Zorn GT, Muehlebach G, Vacek J, Sue Min Lai, Lakkireddy D. Atrial fibrillation following open heart surgery: long-term incidence and prognosis. J Interv Card Electrophysiol. 39(1) (2014) 69-75. doi: 10.1007/s10840-013-9830-6.

5. Phan K, Khuong JN, Xu J, Kanagaratnam A, Yan TD. Obesity and postoperative atrial fibrillation in patients undergoing cardiac surgery: Systematic review and meta-analysis. Int J Cardiol. 217 (2016) 49–57. doi:10.1016/j.ijcard.2016.05.002

6. Nakai T, Lee RJ, Schiller NB, et al. The relative importance of left atrial function versus dimension in predicting atrial fibrillation after coronary artery bypass graft surgery. Am Heart J. 143(1) (2002) 181–186. doi:10.1067/mhj.2002.120294.

7. Parente EB. Is body mass index still a good tool for obesity evaluation? Arch Endocrinol Metab. 60(6) (2016) 507–509. doi:10.1590/2359-3997000000232.

8. Magne J, Salerno B, Mohty D, et al. Echocardiography is useful to predict postoperative atrial fibrillation in patients undergoing isolated coronary bypass surgery: A prospective study. Eur Heart J Acute Cardiovasc Care. 8(2) (2019) 104–113. doi:10.1177/2048872616688419.

9. Lee J, Jang I. Predictors Affecting Postoperative Atrial Fibrillation in Patients After Coronary Artery Bypass Graft [published online ahead of print, 2018 Oct 31]. Clin Nurs Res. 2018;1054773818809285. doi:10.1177/1054773818809285..

10. Le Tourneau T, Messika-Zeitoun D, Russo A, et al. Impact of left atrial volume on clinical outcome in organic mitral regurgitation. J Am Coll Cardiol. 56(7) (2010) 570–578. doi:10.1016/j.jacc.2010.02.059

11. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging [published correction appears in Eur Heart J Cardiovasc Imaging. 2016 Apr;17(4):412] [published correction appears in Eur Heart J Cardiovasc Imaging. 2016 Sep;17 (9):969]. Eur Heart J Cardiovasc Imaging. 16(3) (2015) 233–270. doi:10.1093/ehjci/jev014
12. Osranek M, Fatema K, Qaddoura F, et al. Left atrial volume predicts the risk of atrial fibrillation after cardiac surgery: a prospective study. J Am Coll Cardiol. 48(4) (2006) 779–786. doi:10.1016/j.jacc.2006.03.054.

13. Simopoulos V, Tagarakis G, Hatziefthimiou A, et al. Effectiveness of aldosterone antagonists for preventing atrial fibrillation after cardiac surgery in patients with systolic heart failure: a retrospective study. Clin Res Cardiol. 104(1) (2015) 31–37. doi:10.1007/s00392-014-0754-7

14. Packer M. Epicardial Adipose Tissue May Mediate Deleterious Effects of Obesity and Inflammation on the Myocardium. J Am Coll Cardiol. 71(20) (2018) 2360–2372. doi:10.1016/j.jacc.2018.03.509.

15. Mahajan R, Nelson A, Pathak RK, et al. Electroanatomical Remodeling of the Atria in Obesity: Impact of Adjacent Epicardial Fat. JACC Clin Electrophysiol. 4(12) (2018) 1529–1540. doi:10.1016/j.jacep.2018.08.014