

Impact of Readmissions on Long-term Mortality of Patients Undergoing Cardiac Surgery

El impacto de las reinternaciones en la mortalidad alejada de los pacientes operados de cirugía cardíaca

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ABSTRACT

Background: Readmissions after cardiac surgery are a relevant issue both for patients and the health care system in general. There are limited data about the relationship between readmissions after cardiac surgery and patient prognosis, or their impact on long-term mortality.

Objective: The aim of this study was to analyze the incidence and the predictive factors of 30-day readmissions after cardiac surgery and their association with long-term mortality.

Methods: The Division of Cardiac Surgery computerized database was retrospectively analyzed. The analysis included all consecutive patients undergoing cardiac surgery, discharged during the period between June 2010 and May 2013. Patients undergoing heart transplantation were excluded from the study. Readmission was defined as unplanned hospital admission within 30 days following discharge. Cardiovascular or non-cardiovascular death 30 days after discharge and until the end of follow-up period was considered as long-term mortality.

Results: A total of 1,327 patients were included in the study and 184 (13.9%) were readmitted to hospital. Median follow-up was 826 days (IQR 581 to 1,085 days). Readmitted patients presented higher rate of comorbidities, as chronic obstructive pulmonary disease (6.5% vs. 2.1%; $p=0.002$) and heart failure (12% vs. 6%; $p=0.0064$). Also, in this group there was greater incidence of postoperative complications, as atrial fibrillation (35% vs. 19%; $p<0.0001$) and low cardiac output (9.2% vs. 4%; $p=0.004$). Infections (not mediastinitis) (25%), arrhythmias and permanent pacemaker implantation (15.2%), heart failure (13%), pleural effusion (6.5%), pericardial effusion (3.8%), fever of unknown origin (3.26%) and mediastinitis (6%), among others, were the most frequent causes of readmission. Logistic regression analysis showed that the factors associated with greater risk of readmission were cardiac surgery not involving coronary artery bypass grafting (OR 2.29; 95% CI 1.55-3.37; $p<0.0001$), history of pulmonary disease (OR: 2.95; 95% CI 1.32-6.6; $p=0.0084$), atrial fibrillation (OR 1.99; 95% CI 1.34-2.94; $p=0.0005$) and body mass index (OR 1.046; 95% CI 1.008-1.085; $p=0.017$). Considering the primary endpoint, readmissions were significantly associated with increased mortality at 1 and 3 years: 8.7% vs. 2.3%; $p<0.0001$ and 13.6% vs. 4.2%; $p<0.0001$, respectively.

Conclusions: Readmission within 30 days after cardiac surgery is significantly associated with long-term mortality. The implementation of adequate care measures could reduce the probability of readmissions and, hence, improve the prognosis of this group of patients.

Key words: Thoracic Surgery - Length of Stay - Hospitalization - Mortality

RESUMEN

Introducción: Las reinternaciones posteriores a una cirugía cardíaca son un problema relevante para los pacientes y para el sistema de salud en general. Existen pocos datos respecto de la relación entre las reinternaciones después de cirugía cardíaca y el pronóstico evolutivo de los pacientes, ni de su impacto en la mortalidad alejada.

Objetivos: Analizar la incidencia, los factores predictores de las reinternaciones a 30 días luego de cirugía cardíaca y su asociación con la mortalidad alejada.

Material y métodos: Se analizó en forma retrospectiva la base de datos informatizada del Servicio de Cirugía Cardíaca. En el análisis se incluyeron todos los pacientes sometidos a cirugía cardíaca en forma consecutiva, dados de alta en el período comprendido entre junio de 2010 y mayo de 2013. Se excluyeron los pacientes operados de trasplante cardíaco. Se definió reinternación como el reingreso hospitalario no planificado dentro de los 30 días transcurridos desde su egreso. Fue considerada mortalidad alejada la muerte de causa cardiovascular o no cardiovascular a partir del día 30 posterior al alta, hasta finalizar el seguimiento.

Resultados: Se incluyeron 1327 pacientes, de los cuales fueron reinternados 184 (13,9%). La mediana de seguimiento fue de 826 días (IQ 581 a 1085 días). Los pacientes reinternados presentaban mayor tasa de comorbilidades como EPOC (6,5% contra 2,1%; $p=0,002$) e insuficiencia cardíaca (12% contra 6%; $p=0,0064$). También, en este grupo se observó mayor incidencia de las complicaciones posoperatorias de fibrilación auricular (35% contra 19%; $p<0,0001$) y de bajo gasto cardíaco posoperatorio (9,2% contra 4%; $p=0,004$). Entre las causas más frecuentes de las reinternaciones se identificaron las infecciones (no mediastinitis) (25%), arritmias

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e implante de MCP (15,2%), insuficiencia cardíaca (13%), derrame pleural (6,5%), derrame pericárdico (3,8%), fiebre sin foco establecido (3,26%) y mediastinitis (6%), entre otras. Según el análisis de regresión logística los factores que se asociaban con el mayor riesgo de reinternación fueron la cirugía cardíaca no CRM (IC 95% 1,55-3,37; $p < 0,0001$), antecedentes de enfermedad respiratoria (IC 95% 1,32-6,6; $p = 0,0084$), fibrilación auricular (OR 1,99; IC 95% 1,34-2,94; $p = 0,0005$) e IMC (OR 1,046; IC 95% 1,008-1,085; $p = 0,017$). En cuanto al punto final, las reinternaciones se asociaron en forma significativa con un aumento en la mortalidad a 1 y 3 años: 8,7% contra 2,3%; $p < 0,0001$ y 13,6% contra 4,2%; $p < 0,0001$, respectivamente.

Conclusiones: La reinternación a 30 días luego de cirugía cardíaca se asocia en forma significativa con mayor mortalidad alejada de los pacientes operados. La implementación de las medidas asistenciales adecuadas podría reducir la probabilidad de las reinternaciones, y, en consecuencia, por ende, mejorar el pronóstico de este grupo de pacientes

Palabras Clave: Cirugía torácica - Tiempo de internación - Hospitalización - Mortalidad

Abbreviations

AAF	Atrial fibrillation	CPB	Cardio-pulmonary bypass
AMI	Acute myocardial infarction	PM	Pacemaker
BMI	Body mass index	PO	Postoperative
CABG	Coronary artery bypass grafting	R	Readmission
CHF	Congestive heart failure		

INTRODUCTION

Readmissions after cardiac surgery are a relevant issue both for patients and the health care system in general. Not only are they disappointing for the patient but also a burden for the health care system that should not be disregarded. They could eventually express some failure in the care processes leading to hospital discharge or in the post discharge ambulatory management of these patients. This, without overlooking the importance complications have during postoperative hospitalizations. Therefore, readmissions are currently considered as one of the most highly rated quality of care criteria. (1)

Readmitted patients usually present with more frailty, more comorbidities and often suffer greater incidence of postoperative complications. Hospital readmissions are also reported to negatively impact on the predictive outcome of patients. (2-4) Over the years, the rate of readmissions after cardiac surgery has remained relatively stable, although there is an important discrepancy among surgical centers, sometimes exceeding 20% of patients undergoing this type of surgery. (5-7)

However, there are few data regarding 30-day readmissions after cardiac surgery and their impact on the predictive outcome of patients, or their association with increased risk of long-term mortality. The purpose of this work was thus to analyze the association between 30-day readmissions after cardiac surgery and their association with long-term mortality.

METHODS

The Division of Cardiac Surgery computerized database was retrospectively analyzed. The analysis included all consecutive patients undergoing cardiac surgery and discharged during the period between June 2010 and May 2013. Patients undergoing heart transplantation were excluded from the study. The analysis neither included post-discharge visits to the emergency department without readmission.

Definitions

Readmission was defined as unplanned hospitalization within 30 days following discharge.

Early readmission was considered as hospitalization within 7 days after discharge and late readmission as admission between 8 and 30 days after discharge.

Statistical analysis

Categorical variables were expressed as percentages and continuous variables as mean and standard deviation, as appropriate. Patients' characteristics were compared using the chi-square test for categorical data and Student's *t* test for normal distribution or the non-parametric Mann-Whitney *U* test for non-normal distribution of continuous variables. Significance was established at $p < 0.05$. Survival curves were built using the Kaplan-Meier method and patients with and without readmission were compared with the Log-Rank test. Readmission predictors were evaluated using a logistic regression model including significant variables from univariate models and odds ratios were calculated with their corresponding 95% confidence interval. A Cox regression model adjusted for significant variables of univariate models was built to analyze predictors of long-term mortality and hazard ratios were calculated with their corresponding 95% confidence interval. IBM SPSS Statistics 20 and Stata 12 statistical packages were used for statistical analyses.

Ethical considerations

The study was evaluated and approved by the institutional Ethics Committee.

RESULTS

A total of 1,327 consecutive patients undergoing cardiovascular surgery between June 2010 and May 2013 were retrospectively analyzed, among which 184 (13.9%) were readmitted to hospital. Patients were followed-up for 3 years, with a median of 826 days (IQR 581-1085 days). Median hospital stay was 7 days (IQR 5-11 days) with in-hospital mortality of 5.1% (72 patients). Total mortality during follow-up was 5.5% (73 patients).

The group of patients that were readmitted compared with those that were never readmitted showed that the first group included older patients (67 vs. 65 years of age; $p = 0.029$), greater proportion of women

(36.4 vs. 23.7%; $p=0.0002$), higher body mass index (BMI) (28.6 vs. 27.8; $p=0.02$) and greater surgical risk factors according to the EuroScore (5.4 vs. 4.2; $p=0.0001$). It was also seen that cardiopulmonary bypass (CPB) was more prevalent in the group of re-admitted patients (70% vs. 47%; $p<0.0001$) with a lower ratio of single coronary artery bypass grafting (CABG) procedures (29.4% vs. 51.8%; $p<0.0001$). It is relevant to point out that only 3.34% of CABG were performed using CPB with no difference in its duration between both groups.

Readmitted patients had longer hospital stay (12.3 days vs. 9.8 days; $p=0.026$) with greater postoperative hospitalization (9 days vs. 7.3 days; $p=0.0058$). Median readmission stay was 4 days (IQR 2 to 8 days), with a mean early stay of 4 ± 1.9 days vs. 15 ± 6 days in the case of long-term readmission (Table 1).

Preoperative clinical history: Readmitted patients presented greater rate of comorbidities: chronic obstructive pulmonary disease (EPOC) (6.5% vs. 2.1%; $p=0.002$), congestive heart failure (CHF) (12% vs. 6%; $p=0.0064$), and also greater prevalence of anemia (8.7% vs. 4.6%; $p=0.063$) (Table 1).

Postoperative complications: In the group of re-

admitted patients, there was greater incidence of postoperative complications. There were more cases of atrial fibrillation (AF) (35% vs. 19%; $p<0.001$) and low postoperative cardiac output (9.2% vs. 4%; $p=0.004$). In turn, no significant difference was observed in the incidence of perioperative acute myocardial infarction (AMI), bleeding or reoperation for bleeding. Neither were there significant differences in postoperative need for dialysis nor in the incidence of stroke between both groups (Table 2).

Causes for readmission: Infections (not mediastinitis) (25%), arrhythmias and pacemaker (PM) implantation (15.2%), CHF (13%), pleural effusion (6.5%), mediastinitis (6%), syncope (5.5%), anemia (5.3%), pericardial effusion (3.8%), fever of unknown origin (3.26%), and others (16.3%) were the causes for readmission, and were not different between groups with early or late readmission (Figure 1).

Readmission predictors: Logistic regression analysis showed that patients operated on with CPB had 2.28 (95% CI 1.55-3.37; $p<0.0001$) greater risk of 30-day readmission, as those with history of pulmonary disease (2.95, 95% CI 1.32-6.6; $p=0.0084$) and postoperative AF (1.99, 95% CI 1.34-2.94; $p=0.005$). The

Table 1. Patient baseline characteristics

	WITHOUT readmission	WITH readmission	p
Patients, n	1,143 (86.1%)	184 (13.9%)	
Age, years mean (SD)	65.2 (11.2)	67.4 (12.5)	0.0299
BMI, kg/m ² , mean (SD)	27.8 (4.3)	28.6 (4.7)	0.0206
Male sex	872 (76.3%)	117 (63.6%)	0.0002
Surgical priority (urgency)	315 (27.6%)	54 (29.4%)	0.6576
EuroScore, mean (SD)	4.2 (3.0)	5.4 (2.8)	$p<0.0001$
Surgeries with CPB	535 (46.8%)	129 (70.1%)	$p<0.0001$
CPB time, min, mean (SD)	111.5 (40.0)	116.6 (35.8)	0.1350
CABG	592 (51.8%)	54 (29.4%)	$p<0.0001$
Non-CABG surgery	551 (48.2%)	130 (70.7%)	$p<0.0001$
Valvular	239 (20.9%)	51 (27.7%)	
Combined	156 (13.6%)	44 (23.9%)	
Thoracic aorta	82 (7.2%)	17 (9.2%)	
Others	74 (6.5%)	18 (9.8%)	
Prior AMI	301 (26.3%)	40 (21.7%)	0.2036
Prior PCI	161 (14.1%)	25 (13.6%)	0.9094
Prior CABG	28 (2.5%)	8 (4.4%)	0.1434
COPD	24 (2.1%)	12 (6.5%)	0.0021
CRF	62 (5.4%)	11 (6%)	0.7283
Anemia	53 (4.6%)	16 (8.7%)	0.0632
HT	823 (72%)	137 (74.5%)	0.5346
Dyslipidemia	764 (66.8%)	123 (66.9%)	1.0000
Smoking	646 (56.5%)	98 (53.3%)	0.4087
Diabetes mellitus	256 (22.4%)	50 (27.2%)	0.1578
CHF	68 (6.0%)	22 (12.0%)	0.0064
Hospital stay, days, mean (SD)	9.8 (10.0)	12.3 (10.1)	0.026
Postoperative stay, days, mean (SD)	7.3 (9.1)	9 (7.6)	0.0058

SD: Standard deviation. BMI: Body mass index. CPB: Cardiopulmonary bypass. CABG: Coronary artery bypass grafting. AMI: Acute myocardial infarction PCI: Percutaneous coronary intervention. COPD: Chronic obstructive pulmonary disease. CRF: chronic renal failure. HT: Hypertension. CHF: Congestive heart failure

chance of readmission increased 4.6% (OR 1.046; 95% CI 1.008-1.085; $p=0.017$) for each 1 point increase in BMI. Neither female sex nor age seemed to increase the risk of readmission (Table 3).

Long-term mortality and predictors: Regarding the final endpoint, readmissions were significantly associated with increased mortality at 1 and 3 years (8.7% vs. 2.3%; $p<0.0001$ and 13.6% vs. 4.2%; $p<0.0001$, respectively).

The multivariate analysis, performed to determine the variables predicting reduced survival at 3 years, showed that 30-day readmission after cardiac surgery was significantly associated with worse outcome (HR 3.18; 95% CI 1.93-5.25; $p<0.001$). Older age, need for postoperative dialysis and longer postoperative stay also increased the risk of greater long-term mortality (Table 4).

DISCUSSION

The present work analyzes readmissions after cardiac surgery and their impact on patient outcome. The

main finding of the study is that readmitted patients had significantly shorter survival compared with the group with no readmissions. The need for readmission was significantly associated with 3.18 increase of death risk in the long-term follow-up of operated patients (see Table 4)

Several authors have published studies analyzing the rate of readmissions and their causes in patients undergoing cardiac surgery. (5, 6, 8, 9) According to our knowledge, there are no publications considering the long-term outcome of patients readmitted after cardiac surgery. Hannan et al. found a weak correlation between readmissions in CABG and in-hospital mortality (correlation coefficient 0.32; $p=0.047$). However, this work did not follow-up patients to determine their long-term outcome. (6)

In our study the rate of readmissions was 13.9%, comparable to those reported by other authors. (5, 6, 8) The most prevalent causes for readmission were postoperative infections (not mediastinitis) (25%), arrhythmias and PM implantation (15%), CHF (13%)

	WITHOUT readmission	WITH readmission	p
Patients, n	1,143 (86.1%)	184 (13.9%)	
Perioperative AMI	19 (1.7%)	4 (2.2%)	0.5475
Medical bleeding	91 (8%)	19 (10.3%)	0.3119
Reoperation for bleeding	42 (3.7%)	9 (4.9%)	0.4093
Postoperative LCO	46 (4.0%)	17 (9.2%)	0.0044
AF	217 (19%)	65 (35.3%)	$p<0.0001$
Postoperative dialysis	18 (1.6%)	3 (1.6%)	1.0000
Stroke	10 (0.9%)	1 (0.5%)	1.0000

AMI: Acute myocardial infarction. LCO: Low cardiac output. AF: Atrial fibrillation.

Table 2. Postoperative complications according to presence of readmission

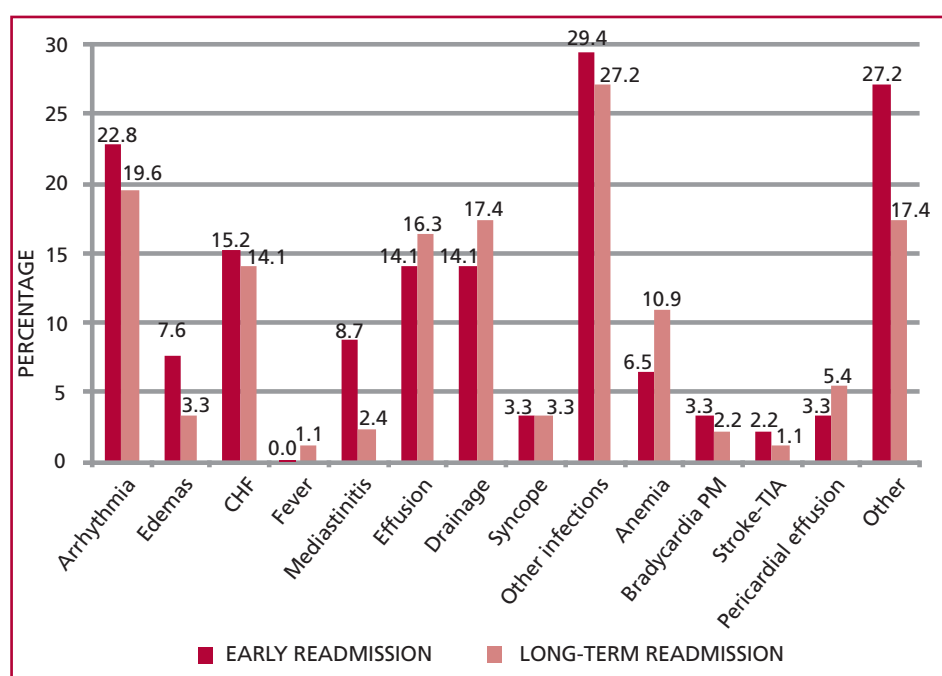


Fig. 1. Causes of early vs. long-term readmissions

CHF: Congestive heart failure. PM: Pacemaker. TIA: Transient ischemic attack.

Table 3. Multivariate analysis of readmission predictors.

	Odds Ratio	95% CI		p
Sex	1.354	0.918	1.998	0.1261
Age	1.003	0.987	1.02	0.6768
Non-CABG surgery	2.287	1.552	3.37	P<0.0001
AF complications	1.993	1.349	2.944	0.0005
History of respiratory disease	2.953	1.32	6.606	0.0084
BMI	1.046	1.008	1.085	0.0171

AMI: Acute myocardial infarction. LCO: Low cardiac output. AF: Atrial fibrillation.

Table 4. Multivariate analysis of long-term mortality

	Hazard Ratio	95% CI		p
Readmission	3.187	1.932	5.258	<0.0001
Age	1.039	1.015	1.063	0.0013
Dialysis at discharge	5.027	2.121	11.916	0.0002
Postoperative stay	1.033	1.021	1.045	<0.0001

CI: Confidence interval.

and pleural effusion (6.5%). In turn, the variables most significantly associated with increased risk of readmission were high BMI (2.95 times greater risk), surgeries with CPB (2.28 times) and presence of AF in the postoperative period (1.99 times). Different from other publications, neither sex nor age evidenced sufficient predictive power. All these data can be especially useful at the moment of designing strategies to reduce readmissions.

When analyzing the differential characteristics of both groups, we found that readmitted patients had greater rate of comorbidities and their immediate postoperative outcome had been more torpid (see Table 1). Different studies reported a prevalence of women, older age and comorbidities, with higher incidence of overweight, anemia and COPD, in readmitted patients. (6, 8, 9) These conditions alone have a negative impact on postoperative survival. (2-4) and probably explain, at least in part, a worse long-term evolution of readmitted patients.

Another relevant data that might clarify the negative effect of readmissions is that readmitted patients usually suffer a higher rate of postoperative complications. Respiratory failure, AF, low cardiac output and renal function impairment with need for dialysis occur more frequently in the group of readmitted patients (see Table 2). Prolonged hospital stay has been also associated with increased long-term mortality. (6) We believe that all the aforementioned conditions would express increased vulnerability in this group of patients and might condition their future evolution.

We could sustain that the group of patients enduring readmission would be exposed to a worse outcome, so their earlier identification and preventive conducts should level these risks. For example, Iribarne et al., analyzing a similar population, postulated that care oriented towards patient history and postoperative complications might decrease readmissions and the

associated hospital health service costs. (8)

One of the hypotheses that might explain these results could be that readmissions express an underlying risk of the more vulnerable patient to suffer postoperative complications and this could impact on its worse outcome. Actions oriented to reduce these complications, among other measures, might neutralize this risk, a hypothesis that should be confirmed by further prospective studies.

Based on our findings, focusing efforts on the reduction of perioperative and readmission complications would favorably influence patient prognosis. It would be useful to identify the group of patients with worse predictive evolution, as it would allow concentrating resources destined to their follow-up.

Limitations

A weakness of the present study was its single-center character, although sample size and follow-up were optimal. It should be pointed out that the rate of readmissions was similar to other works, so it might be expected that these results could be extrapolated to other institutions. One of the main limitations of this study is its retrospective nature with the special biases of this type of studies. However, we should clarify that data loading was prospective as a database of the division of cardiovascular surgery was used which was completed at the moment of patient discharge.

CONCLUSIONS

The present study suggests that 30-day readmissions are significantly associated with lower long-term survival of patients undergoing cardiac surgery. Age, postoperative need for dialysis and longer postoperative stay also correlate with readmissions. The implementation of adequate care policies might reduce the probability of readmissions and hence, improve the prognosis of this group of patients.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)
Pablo

2. Surname (Last Name)
Lamelas

3. Date
10-December-2017

4. Are you the corresponding author? ☒ Yes ☐ No

5. Manuscript Title
El impacto de las reinternaciones en la mortalidad alejada de los
pacientes operados de cirugía cardíaca

6. Manuscript Identifying Number (if you know it)

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Dr. Lamelas has nothing to disclose.

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Section 1. Identifying Information

1. Given Name (First Name)

Juan

2. Surname (Last Name)

Espinoza

3. Date

10-December-2017

4. Are you the corresponding author?

☒ Yes ☐ No

5. Manuscript Title

El impacto de las reinternaciones en la mortalidad alejada de los
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Section 1. Identifying Information

1. Given Name (First Name)

Mariano

2. Surname (Last Name)

Vrancic

3. Date

10-December-2017

4. Are you the corresponding author?

☒ Yes ☐ No

5. Manuscript Title

El impacto de las reinternaciones en la mortalidad alejada de los
pacientes operados de cirugía cardíaca

6. Manuscript Identifying Number (if you know it)

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Section 1. Identifying Information

1. Given Name (First Name)

Fernando

2. Surname (Last Name)

Piccinini

3. Date

10-December-2017

4. Are you the corresponding author?

☒ Yes ☐ No

5. Manuscript Title

El impacto de las reinternaciones en la mortalidad alejada de los
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6. Manuscript Identifying Number (if you know it)

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Mariano

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Camporrotondo

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10-December-2017

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☒ Yes ☐ No

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Non-Financial Support: Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc.

Other: Anything not covered under the previous three boxes

Pending: The patent has been filed but not issued

Issued: The patent has been issued by the agency

Licensed: The patent has been licensed to an entity, whether earning royalties or not

Royalties: Funds are coming in to you or your institution due to your patent

ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)
Daniel

2. Surname (Last Name)
Navia

3. Date
10-December-2017

4. Are you the corresponding author? ☒ Yes ☐ No

5. Manuscript Title
El impacto de las reinternaciones en la mortalidad alejada de los
pacientes operados de cirugía cardíaca

6. Manuscript Identifying Number (if you know it)

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? ☐ Yes ☒ No

Section 3. Relevant financial activities outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the "Add +" box. You should report relationships that were **present during the 36 months prior to publication**.

Are there any relevant conflicts of interest? ☐ Yes ☒ No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? ☐ Yes ☒ No

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Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

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At the time of manuscript acceptance, journals will ask authors to confirm and, if necessary, update their disclosure statements. On occasion, journals may ask authors to disclose further information about reported relationships.

Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Dr. Navia has nothing to disclose.

Evaluation and Feedback

Please visit <http://www.icmje.org/cgi-bin/feedback> to provide feedback on your experience with completing this form.

ICMJE Form for Disclosure of Potential Conflicts of Interest

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in six parts.

1. Identifying information.

2. The work under consideration for publication.

This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check "Yes".

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This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

5. Relationships not covered above.

Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.

Definitions.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name)

Mariano

2. Surname (Last Name)

Benzadon

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10-December-2017

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☒ Yes ☐ No

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Section 6.

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Dr. Benzadon has nothing to disclose.

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