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Title "The effect of surgical delay after hip fracture on mortality. A retrospective survival analysis of 27,397 surgeries in Argentina"

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The effect of surgical delay after hip fracture on mortality

A retrospective survival analysis of 27,397 surgeries in Argentina

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Abstract

Objective: To study the effect of surgical delay after hip fracture on mortality rate in Argentina. *Methods:* We retrieved data of 27,397 patients (79.6% women, age $>= 60$) undergoing surgery after hip fracture from Jan 1, 2011 to Dec 31, 2015 and followed up until Dec 31, 2016. The effect of surgical delay on mortality rates after 1, 2, 3, 6 and 12 months as well as the overall in-sample mortality rate was assessed with a multivariate Cox regression, controlling for age, gender, region, hospital characteristics and 24 comorbidities at baseline. *Results:* Mean surgical delay was 5.95 days and mean follow-up was 764 days. One-year mortality was 15.4% when delay < 3 days and 19.9% for delay $>= 3$ days. Surgical delay, age and male sex were found to significantly increase death risk after one year from admission to hospital—Hazard ratio (HR): 1.025 per additional day of delay (standard error = 0.002), p-value<0.001; HR: 1.056 per additional year (0.002), p<0.001; HR: 1.526 (0.043), p<0.001; respectively. *Conclusion:* Delay from hospital admission to surgery after hip fracture increases mortality in both the short and long run.

Introduction

A hip fracture is a break in the proximal end of the femur at the hip joint. It is a serious injury that requires immediate medical attention. Hip fractures most commonly occur from a trauma like a fall or a direct blow to the side of the hip. Some pathological conditions like osteoporotic disease, poor vision and neurologic-related physical unstableness are between the main risk factors. As of 2000, there were around 1.6 million hip fractures worldwide, with women accounting for 75% of cases.

There are three types of hip fracture depending on what part of the upper femur is involved: intracapsular—at the level of the head and neck of the femur, generally within the capsule (soft-tissue envelope that contains the lubricating fluid of the hip joint), pertrochanteric—between or through the greater and lesser trochanters (the bony protuberances next to and below the neck of the femur respectively)—and subtrochanteric—below the lesser trochanter, where the shaft of the femur begins.

The indicated treatment is surgery. Depending on the type of fracture, two procedures are used: arthroplasty—total or partial replacement of the joint with prosthetic parts made of metal or ceramic—and internal fixation—stabilization with surgical screws, nails, rods, or plates.

Mortality rate after one year of admission to hospital range between 20% and 25%. Increasing age, male gender and greater American Society of Anesthesiologists (ASA) grade are usually related to higher death odds.[1] The effect of surgical delay on mortality rate was largely studied around the world, with varying results. However, there are no papers studying this relationship in Argentina, to the extent of our knowledge. In fact, there are almost no papers about hip fracture in our country at all but only a few studying incidence rates only from an epidemiological standpoint in isolated provinces or hospitals.

The objective of this study is to statistically as-

[1] The ASA score is a six-point pre-surgical assessment that indicates the general health status before undergoing surgery.

sess the effect of surgical delay on mortality rate in Argentina, controlling for all relevant covariates such as age, gender, region, type of hospital and chronic morbidities at baseline. Our hypothesis is that late surgery increases death odds. Because of the high incidence and mortality rates of hip fracture and its related high costs of treatment, this is an important public health question to answer.

Background

The three most frequent methods in the literature to evaluate the effect of surgical delay after hip fracture on mortality are: mean difference tests between groups, logistic regressions and Cox regressions.

Mean difference test

Rodriguez-Fernandez *et al* (2011) did not find differences on mortality after three and twelve months to be statistically significant in a sample of 185 patients (age >= 70) separated in two delay strata: under two days and over a week—with 1-year mortality rates of 24% and 28% respectively. Griffiths *et al* (2013) studied 60 surgeries (age >= 50) and reported a 1-month mortality rate of 10%, finding surgical delay of more than 72h to be a statistically significant risk factor to adverse outcome. Muhm *et al* (2013) reported a 1-year mortality rate of 23.9% in a sample of 138 patients (age >= 65), grouped by delay under and over a 48h threshold. They did not find surgical delay to be an informative predictor of mortality rate.

Logistic regression

Laubjerg *et al* (2012) found that the risk of in-hospital death increased with surgical delay—odds ratio (OR) = 1.3 per additional day, ASA score—OR = 2.3 per point added, male sex—OR = 2.2—and age—OR = 1.4 per 5 years, in a sample of 38,020 patients (age >= 65). Bretherton *et al* (2015) separated 6,236 patients (age >= 60) in seven surgical delay strata: under 6 hours, 7-12h, 13-18h, 19-24h, 25-36h, 37-48h, 49-72h. After controlling for age, sex, ASA score and mobility score, surgery under 12 hours improved 30-day survival compared with surgery over 12 hours. Beyond this threshold, survival rate was not affected by increasing delay.

Cox regression

Vidal et al (2012) reported a 1-year mortality rate of 13.4% from admission in a sample of 343 patients (age >= 60). Increased time from fracture to hospital admission was associated with reduced survival to hospital discharge, but they did not find the delay from admission to surgery to be related with reduced survival rate. Li et al (2014) did not find statistically significant differences between patients having surgery before and after two days from admission in a sample of 499 patients (age >= 50). However, they found the delay from injury to hospitalization to be an important predictor of early mortality rate after hip fracture. Lund et al (2014) reported a 1-year mortality rate of 30%. Surgical delay and time of surgery were not significantly associated with mortality after two, six and twelve months. Colais et al (2015) found that patients who underwent surgery within two days had lower 1-year mortality compared to those who waited for surgery more than two days (HR: 0.83) in a sample of 359,529 patients (age >= 65), after controlling for age, gender and risk factors. Bohm et al (2015) found that patients having surgery before two days had a lower risk of death both in hospital (HR: 0.51) and after a year from admission (HR: 0.72) in a sample of 6,532 patients (age >= 50). In-hospital mortality rate decreased from from 9.6% to 6.8%.

Methods

Data source

We collected hip surgery micro data from the National Institute of Social Services for Retirees and Pensioners (INSSJP, for its initials in Spanish). The INSSJP—aka PAMI—is a government-run medical insurance institution established in Argentina, created to provide healthcare and social services to the elderly. It is the biggest medical insurance organization of Latin America, granting healthcare to 4.8 million people across the country throughout its 38 branches and more than 650 proximity agencies.[2]

Health contractors—both private clinics and public hospitals—electronically transmit information on diagnoses—International Classification of Diagnoses 10th review (ICD-10), medical practices, hospital admissions, medications, medical supplies and prosthesis provided to patients through an online database management system (DBMS). Inputs to this online DBMS feed a relational database with Oracle® architecture where we retrieved data from.

Within this database, each person is assigned a unique ID number which allows to cross match against different systems and applications. In this way, we could retrieve for each registry data on: contractor ID, type of contract, patient ID, branch—used to define regional indicators, rural indicator, gender, date of birth—used for age at admission, date of death, date of admission to hospital and date of surgery—both used for surgical delay, and 24 binary variables indicating the presence on chronic diseases at baseline—inferred from drugs dispensed to patients prior to their admission to hospital.

Contractors

During the span of time of the study, three different types of contracts with health providers coexisted:

i) Per Capita (PC): contractors get a monthly registry of patients assigned for each health provision unit or *module*, defined as a group of practices from the Nomenclature of Medical Provisions. Each module has a single price taking into account the prices and rates of use of each medical practice inside.[3] The monthly payment then consists of the sum across all modules of each quantity of patients times each price, regardless of the medical practices done. However, contractors might qualify to receive an incentive fee if they electronically transmit information on the practices provided.

ii) Hip Fracture Program (HFP): this is a special case of PC. If PC contractors sign up for this program, they receive a supply of prostheses from the Institute in advance so that they do not have to fund the cost and get the prosthesis for each patient admitted with hip fracture. Therefore, this program works as an insurance for contractors, as hip surgery is a high cost practice with low frequency and high volatility of use. The cost of the enrollment is deducted from the monthly contractor's payment.[4]

iii) Electronic Transmission (e-trans.): in opposition to PC payment, contractors get paid solely by medical practices transmitted trough the online DMBS. As there are no lower or upper bounds to billing as in per capita contracts, this payment method involves establishing statistical audit and validations rules so that only feasible practices can be transmitted, taking into account both physical and medical criteria.

These three types of contract as defined above are exhaustive and mutually exclusive in a monthly basis. Both PC and HFP existed prior to this study, while e-trans. was launched in the last quarter of 2013. It is not possible to go back to PC contracts from HFP or e-trans. contracts.

Contractors were also stratified by their size, defined by the quantity of surgeries performed per year, as: "small"—0-12, "medium"—13-24, and "large"—25+.

Patients

From the INSSJP's database, we retrieved information on 30,592 admissions to an acute care hospital for patients diagnosed with a hip fracture—ICD-10 diagnosis codes S72.0 (intracapsular), S72.1 (pertrochanteric) and S72.2 (subtrochanteric)—with admission dates ranging between January 1, 2011 and December 31, 2015 and followed up until December 31, 2016. All patients were 60 or more years old at the time of admission to hospital.

[2] More about INSSJP: http://www.pami.org.ar/

[3] As an example, hip replacement is a surgical practice included in module No. 12 "Admission Module". This module includes in its cost all services provided to patients during their admission, such as medical practices, diagnostic studies, laboratory analyses and the stay itself. The complete Nomenclature can be found in .xls and .pdf at: http://www.pami.org.ar/bot_nomenclador_unico.php

[4] In this case, contractors get assigned on the module No. 90 "Hip Fracture Module" the same registry of patients they have on the module No. 12, and its price is negative, thus subtracting a portion from their PC payment for the Admission Module.

We deleted the following observations containing errors: 4 duplicates, 34 observations with death date prior to admission date—no observations were found with surgery date prior to admission date, 686 surgeries with 2 different admission dates—1372 registries deleted, 1 surgery with 3 different admission dates—3 registries deleted, 10 surgeries with 2 different branches—20 registries deleted, 11 surgeries with 2 different contractors—22 registries deleted, 103 admissions with 2 different surgery dates—206 registries deleted.

Then we excluded pathological cases and outliers to our study: 6 surgical deaths—admission date = surgery date = death date, 65 patients with 3 surgeries—195 registries deleted, 7 patients with 4 surgeries—28 deleted registries, 523 admissions with a surgical delay of more than one month, 782 patients with 2 surgeries—in each case, the first surgery was deleted and a binary indicator of a previous one was created, keeping the last surgery by patient and deleting 782 registries with the first ones. **Figure 1** summarizes the filtering process for our dataset.

Similar to literature, we divided patients in two strata: under 3 days and 3+ days of surgical delay from admission.

Statistics

Mortality rates from admission for 1, 2, 3, 6 and 12 months, as well as for the overall sample, were reported for each delay stratum. We assessed the difference in death proportions between delay strata with a Pearson's χ^2 test.

The relationship between surgical delay and all six mortality rates was assessed using the Cox proportional hazards model. Two different specifications of our multivariate model were estimated: taking surgical delay as an integer variable and as a binary—stratified in two gropus—variable. Kaplan-Meier survival functions where plotted to assess the good behaviour of Cox model in our dataset.

All counts and estimates are shown as numbers without any punctuation markings, while proportions and standard errors in parentheses and confidence intervals in brackets. One asterisk indicates $p < 0.05$, two asterisks $p < 0.01$ and three asterisks $p < 0.001$.

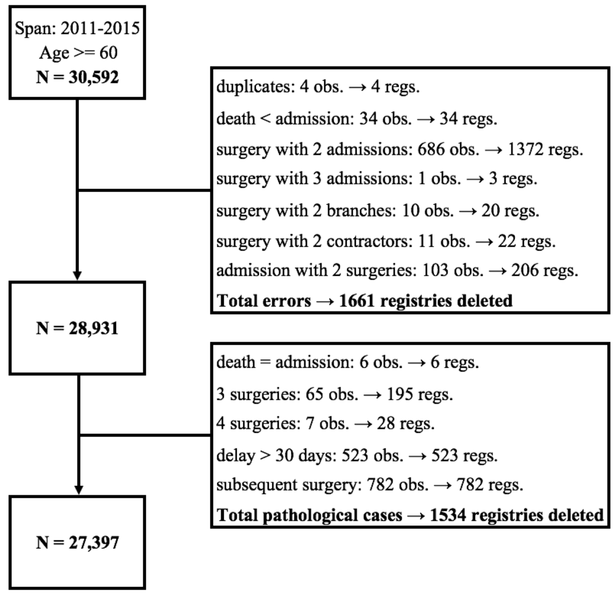

Fig. 1 Dataset filtering process

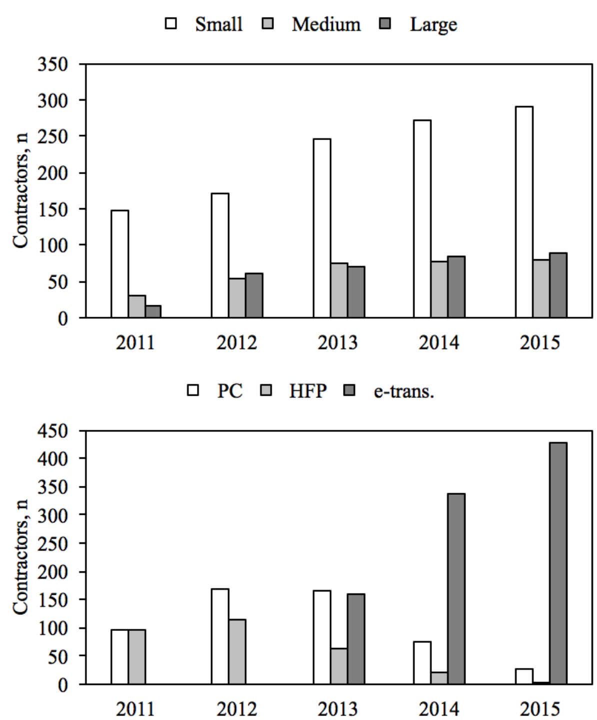

Fig. 2 Active contractors per annum by size—above and contract type—below.

Table 1 Demographics by delay strata, n (%)

Patient characteristic	delay = 0-2 n = 7,799		delay = 3+ n = 19,598	
Age, $\bar{x}$ (sd)	80.9	(7.9)	81.4	(7.6)
Age strata				
60-69	775	(9.9)	1,534	(7.8)
70-79	2,359	(30.3)	5,747	(29.3)
80-89	3,578	(45.9)	9,632	(49.2)
90+	1,087	(13.9)	2,685	(13.7)
Gender				
Females	6,158	(79.0)	15,646	(79.8)
Males	1,641	(21.0)	3,952	(20.2)
Region				
Metro	2,172	(27.8)	10,656	(54.4)
Pampa	4,539	(58.2)	6,883	(35.1)
Cuyo	563	(7.2)	981	(5.0)
Northwest	262	(3.4)	453	(2.3)
Northeast	223	(2.9)	401	(2.1)
Patagonia	40	(0.5)	224	(1.1)
Residence				
Urban	6,451	(82.7)	17,520	(89.4)
Rural	1,348	(17.3)	2078	(10.6)

All statistical analysis and calculations were performed using Stata® statistical software, 13th release.

Results

Contractor characteristics

There were 568 performing contractors during the study time, not all of them active every single year. **Figure 2** plots contractor count per annum both by size and contract type. The quantity of providers grew evenly among all three sizes, being "small" the bigger group, accounting for more than 60% of contractors every year. By contract type, on the contrary, most PC and HFP contractors swapped into e-trans. contractors. As PC and HFP contracts accounted each for 50% of active contracts in 2011, 93% of active contracts in 2015 were e-trans.

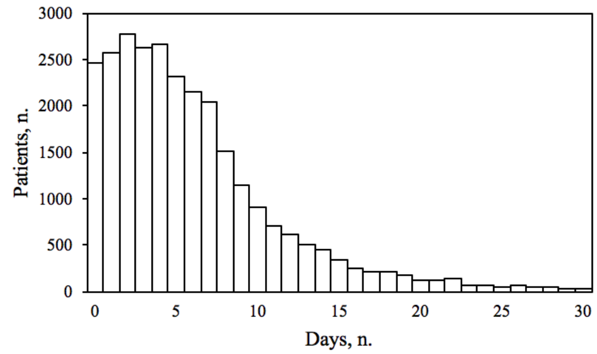

Fig. 3 Frequency histogram of surgical delay. Each column represents the quantity of patients operated at each time frame from admission to hospital—e.g. the first column indicates the frequency of patients that underwent surgery the same day of admission.

Demographics

A total of 27,397 patients underwent hip surgery, 79.6% of which were women. The mean age was 81.7 (7.6) for females and 79.3 (7.7) for males. We found the highest frequency of cases on the eighth decade, with 50.2% for women and 40.6% for men. **Table 1** summarizes patient demographics by delay strata. There were 28.4% of surgeries performed before 3 days from admission. We found no significant differences on age or gender between groups.

Surgical delay

We defined surgical delay as the quantity of full calendar days—integer floor—from admission to hospital until surgery, as we did not have data on time of surgery for most observations. **Figure 3** plots the frequency histogram of surgical delay in our sample.

Table 2 summarizes mean surgical delay sampling statistics by patient and contractor characteristics. The overall average time to surgery was 5.95 days (0.03). Interestingly, the average delay decreased with age. This rather counterintuitive fact could be indicating priority treatment on elder patients—we would expect younger patients to be stabilized and be suitable for surgery earlier than older ones. Mean surgical delay was lower for women—5.91 (0.03) against

Table 2 Mean surgical delay sampling statistics by main patient and contract characteristics—sample size: n, mean: $\bar{x}$, standard error: (se) and 95% confidence interval [CI 95%]

Pat./Contract characteristic	sample n =	mean surgical delay sampling statistics		
Age strata				
60-69	2,309	6.39	(0.13)	[6.14-6.64]
70-79	8,106	6.10	(0.06)	[5.98-6.21]
80-89	13,210	5.92	(0.04)	[5.84-6.01]
90+	3,772	5.50	(0.08)	[5.35-5.66]
Gender				
Females	21,804	5.91	(0.03)	[5.84-5.98]
Males	5,593	6.14	(0.07)	[6.00-6.28]
Size				
Small	4,843	6.03	(0.08)	[5.87-6.20]
Medium	5,590	5.64	(0.07)	[5.50-5.78]
Large	16,964	6.04	(0.04)	[5.96-6.11]
Type				
e-trans.	13,005	5.99	(0.05)	[5.90-6.08]
PC	7,772	6.49	(0.06)	[6.37-6.62]
HFP	6,620	5.25	(0.06)	[5.14-5.36]
Overall	27,397	5.95	(0.03)	[5.89-6.02]

6.14 (0.07) for men, which goes in line with literature.

In terms of contractor characteristics, medium sized providers had the lowest mean surgical delay, while small and large ones had almost no difference. As small contractors could be modestly equipped and large contractors could be overcrowded, this result would be indicating an optimal establishment size along with optimal medical personnel-to-patient ratio. By contract type, HFP scored the lowest average delay at 5.25 (0.06), far behind PC—6.49 (0.06), and e-trans.—5.99 (0.05).

Comorbidities

Table 3 summarizes patient comorbidities at baseline—inferred from dispensed drugs—by delay strata. In line with literature, we found Hypertension to be the most prevalent chronic medical condition on the elderly—being present in around 80% of elder patients, followed by Depression, Epilepsy, Atherosclerosis and Ischemic CVA.

Table 3 Comorbidities by delay strata, n (%). Separated into six categories: cardiovascular, respiratory, neurologic/cognitive, metabolic disorders, osteoarticular, eye diseases. Inferred from dispensed drugs at baseline (i)

Chronic condition	delay = 0-2 n = 7,799		delay = 3+ n = 19,598	
Cardiovascular				
Arrhythmia	1,928	(24.7)	4,336	(22.1)
Atherosclerosis	4,417	(56.6)	10,515	(53.7)
Ischemic (ii)	4,105	(52.6)	10,171	(51.9)
Insufficiency (iii)	3,394	(43.5)	7,989	(40.8)
Hypertension	6,492	(83.2)	15,793	(80.6)
Thrombosis	3,833	(49.1)	8,451	(43.1)
Respiratory				
Asthma	3,124	(40.0)	7,021	(35.8)
COPD (iv)	1,168	(15.0)	2,612	(13.3)
Neurologic				
Alzheimer	2,152	(27.6)	4,968	(25.3)
Dementia	2,553	(32.7)	6,329	(32.3)
Depression	5,498	(70.5)	13,094	(66.8)
Epilepsy	4,539	(58.2)	10,458	(53.4)
Parkinson	945	(12.1)	2,332	(11.9)
Metabolic				
Diabetes	1,833	(23.5)	4,711	(24.0)
Dyslipidemia	3,455	(44.3)	8,064	(41.1)
Hyperthyroidism	39	(0.5)	106	(0.5)
Hypothyroidism	1,812	(23.2)	4,011	(20.5)
Obesity	87	(1.1)	156	(0.8)
Osteoarticular				
Arthritis	4,031	(51.7)	8,324	(42.5)
Arthrosis (v)	3,504	(44.9)	7,788	(39.7)
Gout (vi)	614	(7.9)	1,253	(6.4)
Osteoporosis	2,484	(31.9)	5,351	(27.3)
Rheuma (vii)	3,764	(48.3)	8,683	(44.3)
Ophtalmic				
Glaucoma	1,511	(19.4)	3,466	(17.7)

Notes: (i) We could do this as specific pharmacological actions are indicated only on specific diseases; for example: an antihypertensive drug signals the presence of hypertension on the patient (ii) Ischemic cardio-myopathy—aka ischemic cerebrovascular accident or heart stroke; (iii) Cardiac insufficiency—aka heart failure (iv) Chronic Obstructive Pulmonary Disease—aka chronic bronchitis or pulmonary emphysema (v) aka Osteoarthritis; (vi) aka Inflammatory Arthritis; (vii) Rheumatoid Arthritis.

Table 4 Mortality rates by delay strata—death count: n, death proportion: (%), difference in proportions (Pearson's Chi-squared test)

Death rate at	delay = 0-2 n = 7,799		delay = 3+ n = 19,598		χ^2 test Diff.
1 month	306	(3.9)	725	(3.7)	-.002
2 months	475	(6.1)	1,347	(6.9)	.008*
3 months	680	(8.7)	2,027	(10.3)	.016***
6 months	1,202	(15.4)	3,891	(19.9)	.044***
1 year	1,748	(22.4)	5,573	(28.4)	.060***
Overall	3,031	(38.9)	8,885	(45.3)	.065***

Notes: statistical significance tests: * $p<0.05$, ** $p < 0.01$, *** $p<0.001$

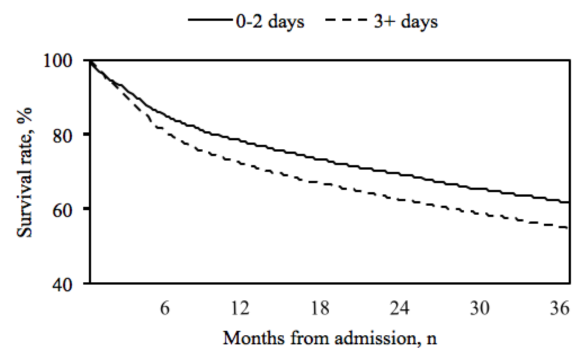

Fig. 4b Kaplan-Meier survival functions by delay strata

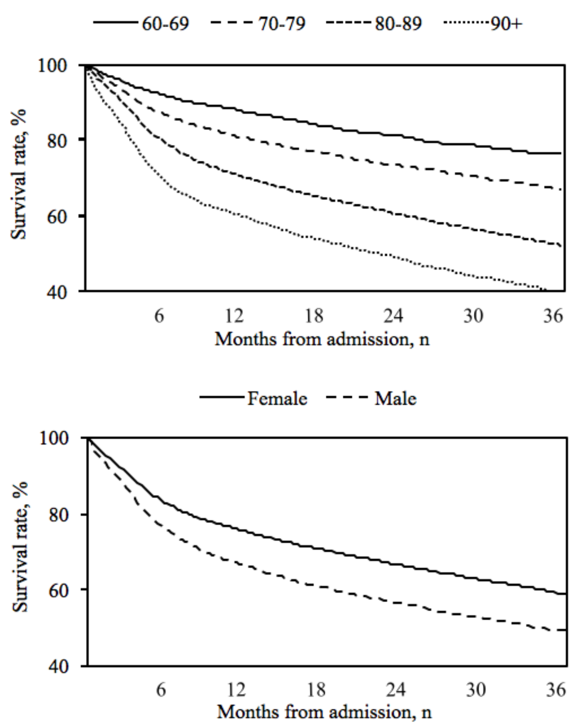

Fig. 4a Kaplan-Meier survival functions by patient characteristics: age—above, and sex—below.

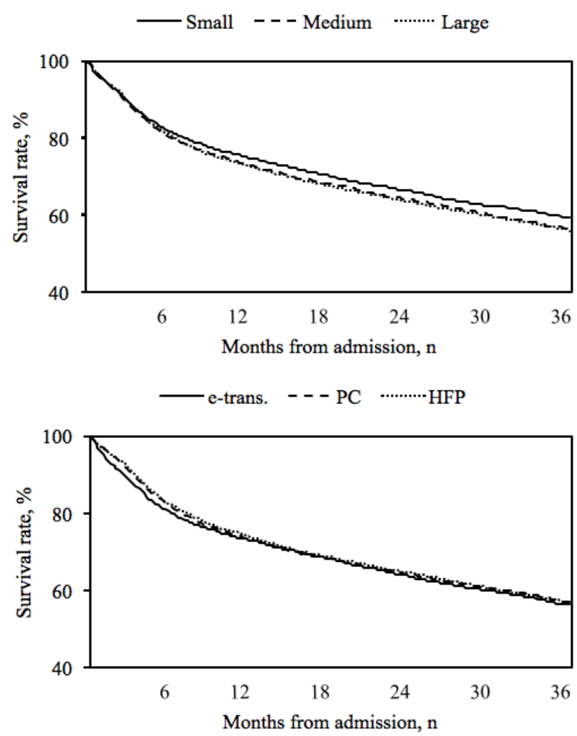

Fig. 4c Kaplan-Meier survival functions by contractor characteristics: size—above, and type—below

Table 5 Multivariate Cox proportional hazards model estimates for 1 year and overall mortality rates, considering delay as both a integer and a categorical variable—hazard ratios (HR), standard errors (se)

Covariates	1 year mortality—deaths = 7,321				Overall mortality—deaths = 11,916			
	Delay: Integer (+1)		Delay: Strata (>=3)		Delay: Integer (+1)		Delay: Strata (>=3)	
Delay	1.025***	(0.002)	1.204***	(0.034)	1.020***	(0.002)	1.164***	(0.025)
Patient								
Age	1.056***	(0.002)	1.055***	(0.002)	1.051***	(0.001)	1.045***	(0.001)
Male	1.526***	(0.043)	1.533***	(0.043)	1.434***	(0.033)	1.438***	(0.033)
Contractor								
PC	0.851***	(0.024)	0.859***	(0.024)	0.856***	(0.020)	0.862***	(0.020)
HFP	0.914**	(0.027)	0.901***	(0.027)	0.928**	(0.022)	0.918***	(0.022)
Medium	1.053	(0.041)	1.039	(0.041)	1.066*	(0.033)	1.056	(0.032)
Large	0.972	(0.035)	0.947	(0.034)	0.989	(0.028)	0.970	(0.027)

Notes: statistical significance tests: * p<0.05, ** p<0.01, *** p<0.001

Survival analysis

Mortality rates from admission are shown in **Table 4**. The difference in overall mortality rate as well as in 3, 6 and 12-month mortality rates was highly statistically significant ($p < 0.001$). Difference in 2-month mortality rate was found to be significant at 5% ($p = 0.019$). On the other hand, the gap in 1-month mortality rates between strata was not statistically significant ($p = 0.379$).

The mean follow-up for each patient was 764 days, with a median of 701 days and a maximum of 2,176 days.

Figures 4a, **4b** and **4c** plot Kaplan-Meier survival functions by patient demographics, delay strata and contractor characteristics respectively. In all cases we found survival functions to be parallel between strata, which goes in line with literature and is often referred as a necessary condition for Cox model suitability.

As expected, survival functions shrank with increasing age and male gender. By contract type all three functions were almost identical, while by size small providers had a somewhat higher survival rate against medium and large ones. In the case of delay strata, shorter surgical delay was associated with higher survival rates in the long run—77.8% vs 71.7% after 12 months, 69.0% vs 62.3% after 24 months and 61.7% vs 54.9% after 36 months.

Table 5 presents Cox regression estimates for 1-year and overall mortality rates including the main covariates—excluding regional and comorbidity dummies. **Tables A1** and **A2** from **Appendix** display complete estimation results for the six model specifications considering delay as an integer and as a categorical variable, respectively—12 model specifications.

We found all covariates but contractor size ones to be statistically significant. Surgical delay was associated with an increased death risk at 1 year from admission—one more day of delay: HR = 1.025 (0.002), delay over 3 days vs. delay under 3 days: HR = 1.204 (0.034). Age—HR = 1.056 (0.002)—and male sex—HR = 1.526 (0.043)—were also associated with higher death probabilities. On the other side, PC and HFP type of contracts were related to lower death risks at 1 year from admission against e-trans. contracts

Discussion

Many papers have emphasized the importance of early surgery in reducing post-operative morbidity and mortality rates. However, varying definitions of "early" surgery—such as before 24h, 48h or 72h from admission to hospital, as well as different follow-up times, sample designs, identifying strategies and covariate sets have led to inconclusive results, as we saw in the background section. For example, some papers on this subject include length of stay as an explanatory variable on mortality. From our standpoint, however, this should be considered as an outcome variable—because part of the stay in hospital takes place after surgery, and thus taking it as a regressor would lead to confounding bias. Other articles lack information on contractor characteristics, which are as important as patient demographics to explain dispersion on delay times.

This is the first study to assess the effect of surgical delay after hip fracture on mortality rates in Argentina, to the extent of our knowledge. As usual in the literature, we included age and sex as explanatory variables. We also included two contractor characteristics: size—defined in terms of quantity of surgical procedures per year—and type—depending on how the payment to the provider is done. As we did not have information on ASA score, we included 24 dummy variables indicating the presence of most common chronic medical conditions on the elderly. Regional indicators were also added to our statistical model. As for surgical delay definition, we addressed the two common approaches: an integer variable and categorical variable, taking 72h as the threshold for early and late surgery. Outcome variables were 1, 2, 3, 6 and 12-month as well as overall in-sample mortality rates.

We found that surgical delay increases mortality odds at two, three, six and twelve months from admission to hospital, as well as in the long run. Each day of additional delay significantly increased death risk at all these endpoints, as well as having a delay of three or more days against a delay under that bound. Older patients and males were also related to higher mortality rates, as expected. PC and HFP contractors had significantly lower mortality rates against e-trans. health providers. Contractor size, on the other size, did not significantly affect mortality rates while it affected surgical timing. Regional variables and morbidity indicators showed mixed results.

Among the strengths of our study we find its nationwide design, the large sample size, the long follow-up time (mean above two years) and the inclusion of contractor characteristics. Among the main weaknesses we find that this is not a population-based study, the integer cutoff for delay days and the lack of ASA score. Regarding the first issue, the INSSJP is a public health insurance organization that provides healthcare to those elder patients that can not afford a private insurance. Hence, lower income decile individuals are included in this study, which might lead to a bias in mortality rates. Out of 6.7 million people 60 or more years old in Argentina as of 2017, 4 million are insured at the INSSJP. With respect to the second weakness, we lacked actual time of operation which led to discrete time delays. This could introduce a bias specially in the delay strata approach because of observations surrounding the selected boundary. As for the last pitfall, we surpassed it by the inclusion of comorbidity dummies.

This article provides an insight into the effects of surgical delay after hip fracture on mortality in our country, despite its limitations. As with any observational study, we should be aware of the potential presence of selection bias. Further research should assess possible endogeneity of surgical delay in the estimated structural equation and propose an identification strategy to deal with it if that was the case.

Conclusion

We found that delay from hospital admission to surgery after hip fractures increases mortality in both the short and long run.

References

1. Aqil, Adeel; Hossain, Fahad; Sheikh, Hassaan; Aderinto, Joseph; Whitwell, George and Kapoor, Harish. "Achieving hip fracture surgery within 36 hours: an investigation of risk factors to surgical delay and recommendations for practice". Journal of Orthopaedics and Traumatology (2016); 17 (3): 207-213.

2. Bohm, Eric; Loucks, Lynda; Wittmeier, Kristy; Lix, Lisa M and Oppenheimer, Luis. "Reduced time to surgery improves mortality and length of stay following hip fracture: results from an intervention study in a Canadian health authority". Canadian Journal of Surgery (2015); 58 (4): 257-263.

3. Bretherton, CP and Parker, MJ. "Early surgery for patients with a fracture of the hip decreases

30-day mortality". The Bone & Joint Journal (2015); 97-B: 104–108.

4. Colais, Paola; Di Martino, Mirko; Fusco, Danilo; Perucci, Carlo A and Davoli, Marina. "The effect of early surgery after hip fracture on 1-year mortality". BMC Geriatrics (2015); 15: 141-148.

5. Griffiths, EJ; Cash, DJW; Kalra, S and Hopgood, PJ. "Time to surgery and 30-day morbidity and mortality of periprosthetic hip fractures". Injury—International Journal of the Care of the Injured (2013), 44 (12): 1949–1952.

6. Laubjerg Daugaard, Cecilie; Jørgensen, Henrik L; Riis, Troels; Lauritzen, Jes B; Duus, Benn R and van der Mark, Susanne. "Is mortality after hip fracture associated with surgical delay or admission during weekends and public holidays? A retrospective study of 38,020 patients". Acta Orthopaedica (2012); 83 (6): 609–613.

7. Li, Yizhong; Lin, Jinkuang; Wang, Peiwen; Yao, Xuedong; Yu, Haiming; Zhuang, Huafeng; Zhang, Linlin and Zeng, Yanjun. "Effect of time factors on the mortality in brittle hip fracture". Journal of Orthopaedic Surgery and Research (2014); 9: 37-41.

8. Lund, Caterina A; Møller, Ann M, Wetterslev, Jørn and Lundstrøm, Lars H. "Organizational Factors and Long-Term Mortality after Hip Fracture Surgery. A Cohort Study of 6143 Consecutive Patients Undergoing Hip Fracture Surgery". PLoS ONE (2014); 9 (6): e99308. doi:10.1371/journal.pone.0099308.

9. Moja, Lorenzo; Piatti, Alessandra; Pecoraro, Valentina; Ricci, Cristian; Virigli, Gianni; Salanti, Georgia; Germagnoli, Luca; Liberati, Alessandro and Banfi, Giuseppe. "Timing Matters in Hip Fracture Surgery: Patients Operated within 48 Hours Have Better Outcomes. A Meta-Analysis and Meta-Regression of over 190,000 Patients". PLoS ONE (2012); 7 (10): e46175. doi:10.1371/journal.pone.0046175.

10. Muhm, M; Arend, G; Ruffing, T and Winkler H. "Mortality and quality of life after proximal femur fracture—effect of time until surgery and reasons for delay". European Journal of Trauma and Emergency Surgery (2013); 39: 267–275.

11. Rodriguez-Fernandez, Pedro; Adarraga-Cansino, Dolores and Carpintero, Pedro. "Effects of Delayed Hip Fracture Surgery on Mortality and Morbidity in Elderly Patients". Clinical Orthopaedics and Related Research (2011); 469: 3218–3221.

12. Ryan, Devon J; Yoshihara, Hiroyuki; Yoneoka, Daisuke; Egol, Kenneth A and Zuckerman Joseph D. "Delay in Hip Fracture Surgery: An Analysis of Patient-Specific and Hospital-Specific Risk Factors". Journal of Orthopaedic Trauma (2015); 29: 343–348.

13. Simunovic, Nicole; Devereaux, PJ and Bhandari, Mohit. "Surgery for hip fractures: Does surgical delay affect outcomes?". Indian Journal of Orthopaedics (2011); 45 (1): 27–32.

14. Uzoigwe, Chika E; Burnand, Henry GF; Cheesman, Caroline L; Osaro Aghedo, Douglas, Faizi, Murtuza and Middleton, Rory George. "Early and ultra-early surgery in hip fracture patients improves survival". Injury—International Journal of the Care of the Injured (2013), 44 (6): 726–729.

15. Vidal, EIO.; Moreira-Filho, DC; Pinheiro, RS; Souza, RC; Almeida, LM; Camargo, KR Jr; Villas Boas, PJF; Fukushima, FB and & Coeli, CM. "Delay from fracture to hospital admission: a new risk factor for hip fracture mortality?". Osteoporosis International (2012); 23: 2847–2853.

Appendix

Tables A1 and **A2** display complete estimation results for the six model specifications in each case: surgical delay as an integer and categorical variable—12 total statistical models.

Table A1 Cox proportional hazards model estimates for 1, 2 and 3-month mortality rates, considering surgical delay as an integer variable—hazard ratio: HR, standard error (se), statistical significance test: *p-value*

Covariates	1-month mortality deaths = 1,031			2-month mortality deaths = 1,822			3-month mortality deaths = 2,707		
Age	1.064	(0.005)	*<0.001*	1.057	(0.004)	*<0.001*	1.057	(0.003)	*<0.001*
Male	1.614	(0.118)	*<0.001*	1.542	(0.086)	*<0.001*	1.508	(0.069)	*<0.001*
Delay	0.990	(0.006)	*0.121*	1.017	(0.005)	*<0.001*	1.019	(0.004)	*<0.001*
Contract type									
PC	0.614	(0.048)	*<0.001*	0.596	(0.035)	*<0.001*	0.684	(0.032)	*<0.001*
HFP	0.650	(0.054)	*<0.001*	0.624	(0.039)	*<0.001*	0.715	(0.036)	*<0.001*
Provider size									
Medium	0.958	(0.097)	*0.674*	0.979	(0.074)	*0.778*	1.020	(0.064)	*0.748*
Large	0.882	(0.082)	*0.175*	0.860	(0.060)	*0.030*	0.887	(0.051)	*0.037*
Region									
Pampa	0.999	(0.076)	*0.986*	0.998	(0.057)	*0.976*	0.972	(0.045)	*0.536*
Cuyo	1.244	(0.171)	*0.113*	1.140	(0.123)	*0.223*	1.0867	(0.098)	*0.357*
NW	1.102	(0.213)	*0.615*	0.965	(0.145)	*0.813*	0.963	(0.121)	*0.764*
NE	0.881	(0.198)	*0.573*	0.733	(0.133)	*0.088*	0.715	(0.109)	*0.027*
Patagonia	0.603	(0.250)	*0.222*	0.928	(0.224)	*0.756*	0.893	(0.182)	*0.580*
Rural	0.835	(0.088)	*0.087*	0.890	(0.070)	*0.140*	0.891	(0.058)	*0.078*
Comorbidities									
Arrhytmia	1.121	(0.088)	*0.146*	1.087	(0.065)	*0.160*	1.083	(0.053)	*0.103*
Atherosclerosis	1.016	(0.092)	*0.862*	0.967	(0.067)	*0.623*	0.933	(0.053)	*0.227*
Ischemic	0.793	(0.053)	*<0.001*	0.821	(0.041)	*0.000*	0.827	(0.034)	*<0.001*
Insufficiency	1.092	(0.076)	*0.211*	1.106	(0.058)	*0.056*	1.118	(0.048)	*0.010*
Hypertension	1.018	(0.089)	*0.837*	1.022	(0.067)	*0.741*	1.034	(0.056)	*0.539*
Thrombosis	0.604	(0.042)	*0.000*	0.680	(0.035)	*<0.001*	0.701	(0.030)	*<0.001*
Asthma	0.884	(0.072)	*0.133*	0.909	(0.056)	*0.121*	0.859	(0.044)	*0.003*
Copd	0.976	(0.113)	*0.837*	0.953	(0.083)	*0.584*	0.981	(0.071)	*0.787*
Alzheimer	1.035	(0.080)	*0.658*	1.041	(0.061)	*0.489*	1.041	(0.050)	*0.398*
Dementia	0.834	(0.063)	*0.019*	0.894	(0.050)	*0.047*	0.917	(0.042)	*0.059*
Depression	0.987	(0.072)	*0.862*	0.999	(0.055)	*0.991*	1.027	(0.047)	*0.560*
Epilepsy	0.915	(0.063)	*0.198*	0.947	(0.049)	*0.295*	0.938	(0.040)	*0.131*
Parkinson	1.144	(0.113)	*0.174*	1.107	(0.083)	*0.175*	1.142	(0.069)	*0.028*
Diabetes	1.191	(0.092)	*0.024*	1.208	(0.070)	*0.001*	1.189	(0.056)	*<0.001*
Dyslipidemia	0.858	(0.080)	*0.099*	0.933	(0.066)	*0.327*	0.971	(0.056)	*0.609*
Hyperthyroidism	1.233	(0.554)	*0.642*	1.367	(0.435)	*0.326*	0.902	(0.286)	*0.745*
Hypothyroidism	0.936	(0.081)	*0.442*	0.936	(0.061)	*0.308*	0.940	(0.050)	*0.242*
Obesity	0.743	(0.335)	*0.510*	0.928	(0.282)	*0.806*	0.854	(0.222)	*0.543*
Arthritis	1.063	(0.077)	*0.397*	0.992	(0.054)	*0.879*	1.023	(0.046)	*0.612*
Arthrosis	0.785	(0.058)	*0.001*	0.728	(0.041)	*<0.001*	0.707	(0.033)	*<0.001*
Gout	0.918	(0.125)	*0.529*	0.859	(0.091)	*0.150*	0.908	(0.077)	*0.258*
Osteoporosis	0.972	(0.079)	*0.723*	0.954	(0.059)	*0.448*	0.922	(0.047)	*0.108*
Rheumatism	0.896	(0.063)	*0.116*	0.863	(0.046)	*0.005*	0.892	(0.038)	*0.008*
Glaucoma	1.210	(0.096)	*0.017*	1.104	(0.068)	*0.110*	1.004	(0.052)	*0.945*

Table A1 (cont.) Cox proportional hazards model estimates for 6-month, 1-year and overall mortality rates, considering surgical delay as an integer variable—hazard ratio: HR, standard error (se), statistical significance test: *p-value*

Covariates	6 -month mortality deaths = 5,093			1-year mortality deaths = 7,321			Overall mortality deaths = 11,916		
Age	1.060	(0.002)	*<0.001*	1.056	(0.002)	*<0.001*	1.051	(0.001)	*<0.001*
Male	1.534	(0.051)	*<0.001*	1.526	(0.043)	*<0.001*	1.434	(0.033)	*<0.001*
Delay	1.026	(0.003)	*<0.001*	1.025	(0.002)	*<0.001*	1.020	(0.002)	*<0.001*
Contract type									
PC	0.794	(0.027)	*<0.001*	0.851	(0.024)	*<0.001*	0.856	(0.020)	*<0.001*
HFP	0.842	(0.030)	*<0.001*	0.914	(0.027)	*0.003*	0.928	(0.022)	*0.002*
Provider size									
Medium	1.055	(0.049)	*0.250*	1.053	(0.041)	*0.192*	1.066	(0.033)	*0.038*
Large	0.925	(0.039)	*0.067*	0.972	(0.035)	*0.430*	0.989	(0.028)	*0.697*
Region									
Pampa	0.915	(0.031)	*0.009*	0.911	(0.026)	*0.001*	0.866	(0.019)	*<0.001*
Cuyo	1.032	(0.068)	*0.634*	0.972	(0.054)	*0.610*	0.951	(0.041)	*0.236*
NW	0.822	(0.081)	*0.047*	0.786	(0.067)	*0.005*	0.793	(0.055)	*0.001*
NE	0.749	(0.081)	*0.008*	0.682	(0.065)	*<0.001*	0.735	(0.054)	*<0.001*
Patagonia	0.790	(0.126)	*0.138*	0.820	(0.108)	*0.131*	0.790	(0.088)	*0.034*
Rural	0.925	(0.044)	*0.105*	0.959	(0.038)	*0.295*	1.045	(0.032)	*0.151*
Comorbidities									
Arrhytmia	1.113	(0.039)	*0.002*	1.111	(0.033)	*<0.001*	1.087	(0.025)	*<0.001*
Atherosclerosis	0.954	(0.039)	*0.248*	1.007	(0.034)	*0.845*	1.024	(0.027)	*0.366*
Ischemic	0.854	(0.025)	*<0.001*	0.893	(0.022)	*<0.001*	0.911	(0.018)	*<0.001*
Insufficiency	1.138	(0.036)	*<0.001*	1.122	(0.029)	*<0.001*	1.172	(0.024)	*<0.001*
Hypertension	0.996	(0.039)	*0.927*	1.016	(0.034)	*0.627*	0.986	(0.026)	*0.600*
Thrombosis	0.726	(0.022)	*<0.001*	0.779	(0.020)	*<0.001*	0.873	(0.017)	*<0.001*
Asthma	0.915	(0.033)	*0.015*	0.895	(0.027)	*<0.001*	0.977	(0.023)	*0.318*
COPD	0.920	(0.049)	*0.113*	0.898	(0.040)	*0.014*	0.917	(0.030)	*0.008*
Alzheimer	0.982	(0.034)	*0.601*	0.988	(0.028)	*0.672*	1.015	(0.022)	*0.492*
Dementia	0.990	(0.033)	*0.753*	1.117	(0.030)	*<0.001*	1.249	(0.026)	*<0.001*
Depression	1.053	(0.035)	*0.122*	1.090	(0.030)	*0.002*	1.097	(0.025)	*<0.001*
Epilepsy	0.923	(0.029)	*0.010*	0.946	(0.025)	*0.034*	0.969	(0.020)	*0.119*
Parkinson	1.176	(0.051)	*<0.001*	1.098	(0.040)	*0.011*	1.116	(0.031)	*<0.001*
Diabetes	1.239	(0.042)	*<0.001*	1.233	(0.035)	*<0.001*	1.191	(0.026)	*<0.001*
Dyslipidemia	0.922	(0.039)	*0.052*	0.884	(0.030)	*<0.001*	0.884	(0.023)	*<0.001*
Hyperthyroidism	1.139	(0.229)	*0.518*	0.872	(0.163)	*0.464*	0.915	(0.122)	*0.506*
Hypothyroidism	0.090	(0.035)	*0.010*	0.895	(0.029)	*0.001*	0.931	(0.023)	*0.003*
Obesity	1.045	(0.181)	*0.801*	1.058	(0.150)	*0.692*	1.024	(0.107)	*0.825*
Arthritis	0.974	(0.032)	*0.423*	0.970	(0.026)	*0.262*	0.984	(0.021)	*0.407*
Arthrosis	0.725	(0.024)	*<0.001*	0.670	(0.019)	*<0.001*	0.718	(0.015)	*<0.001*
Gout	0.992	(0.059)	*0.894*	0.999	(0.050)	*0.977*	1.002	(0.038)	*0.963*
Osteoporosis	0.845	(0.032)	*<0.001*	0.835	(0.026)	*<0.001*	0.851	(0.020)	*<0.001*
Rheumatism	0.904	(0.028)	*0.001*	0.893	(0.023)	*<0.001*	0.925	(0.019)	*<0.001*
Glaucoma	0.964	(0.037)	*0.345*	0.983	(0.031)	*0.592*	0.960	(0.024)	*0.097*

Table A2 Cox proportional hazards model estimates for 1, 2 and 3-month mortality rates, considering surgical delay as a categorical variable—hazard ratio: HR, standard error (se), statistical significance test: *p-value*

Covariates	1-month mortality deaths = 1,031			2 -month mortality deaths = 1,822			3-month mortality deaths = 2,707		
Age	1.064	(0.005)	*<0.001*	1.057	(0.004)	*<0.001*	1.056	(0.003)	*<0.001*
Male	1.611	(0.118)	*<0.001*	1.547	(0.086)	*<0.001*	1.514	(0.069)	*<0.001*
Delay >= 3 days	0.877	(0.062)	*0.063*	1.047	(0.058)	*0.405*	1.102	(0.051)	*<0.001*
Contract type									
PC	0.613	(0.048)	*<0.001*	0.600	(0.035)	*<0.001*	0.689	(0.032)	*<0.001*
HFP	0.652	(0.054)	*<0.001*	0.616	(0.039)	*<0.001*	0.706	(0.036)	*<0.001*
Provider size									
Medium	0.963	(0.098)	*0.708*	0.971	(0.074)	*0.694*	1.010	(0.064)	*0.871*
Large	0.890	(0.082)	*0.207*	0.847	(0.059)	*0.017*	0.871	(0.050)	*0.016*
Region									
Pampa	0.996	(0.075)	*0.952*	0.964	(0.055)	*0.525*	0.943	(0.044)	*0.207*
Cuyo	1.233	(0.170)	*0.130*	1.119	(0.121)	*0.298*	1.072	(0.097)	*0.438*
NW	1.088	(0.211)	*0.664*	0.966	(0.146)	*0.816*	0.970	(0.122)	*0.808*
NE	0.873	(0.196)	*0.545*	0.724	(0.132)	*0.077*	0.711	(0.108)	*0.025*
Patagonia	0.597	(0.247)	*0.212*	0.949	(0.229)	*0.827*	0.916	(0.187)	*0.668*
Rural	0.834	(0.088)	*0.084*	0.885	(0.070)	*0.120*	0.888	(0.058)	*0.066*
Comorbidities									
Arrhytmia	1.122	(0.088)	*0.142*	1.085	(0.064)	*0.168*	1.081	(0.053)	*0.112*
Atherosclerosis	1.017	(0.092)	*0.857*	0.966	(0.067)	*0.615*	0.933	(0.053)	*0.221*
Ischemic	0.793	(0.053)	*0.001*	0.822	(0.041)	*<0.001*	0.828	(0.034)	*<0.001*
Insufficiency	1.092	(0.076)	*0.211*	1.106	(0.058)	*0.056*	1.117	(0.048)	*0.010*
Hypertension	1.019	(0.089)	*0.829*	1.020	(0.067)	*0.764*	1.031	(0.056)	*0.565*
Thrombosis	0.604	(0.042)	*<0.001*	0.677	(0.035)	*<0.001*	0.699	(0.030)	*<0.001*
Asthma	0.883	(0.072)	*0.129*	0.911	(0.056)	*0.130*	0.861	(0.044)	*0.003*
COPD	0.978	(0.113)	*0.848*	0.952	(0.083)	*0.573*	0.979	(0.071)	*0.766*
Alzheimer	1.035	(0.080)	*0.655*	1.039	(0.061)	*0.510*	1.039	(0.050)	*0.417*
Dementia	0.838	(0.064)	*0.020*	0.893	(0.050)	*0.045*	0.915	(0.042)	*0.054*
Depression	0.988	(0.072)	*0.873*	0.996	(0.055)	*0.941*	1.023	(0.046)	*0.610*
Epilepsy	0.914	(0.063)	*0.191*	0.948	(0.049)	*0.306*	0.939	(0.040)	*0.141*
Parkinson	1.144	(0.113)	*0.174*	1.107	(0.083)	*0.174*	1.142	(0.069)	*0.028*
Diabetes	1.190	(0.092)	*0.024*	1.213	(0.070)	*0.001*	1.194	(0.057)	*<0.001*
Dyslipidemia	0.857	(0.080)	*0.097*	0.933	(0.066)	*0.324*	0.971	(0.056)	*0.606*
Hyperthyroidism	1.223	(0.550)	*0.654*	1.370	(0.436)	*0.323*	0.905	(0.287)	*0.752*
Hypothyroidism	0.934	(0.081)	*0.443*	0.935	(0.061)	*0.298*	0.939	(0.050)	*0.234*
Obesity	0.747	(0.336)	*0.517*	0.922	(0.281)	*0.790*	0.848	(0.221)	*0.527*
Arthritis	1.062	(0.077)	*0.404*	0.989	(0.054)	*0.839*	1.021	(0.046)	*0.645*
Arthrosis	0.785	(0.058)	*0.001*	0.727	(0.041)	*<0.001*	0.706	(0.032)	*<0.001*
Gout	0.917	(0.125)	*0.527*	0.858	(0.091)	*0.146*	0.907	(0.077)	*0.251*
Osteoporosis	0.972	(0.079)	*0.724*	0.954	(0.059)	*0.446*	0.921	(0.047)	*0.107*
Rheumatism	0.896	(0.063)	*0.116*	0.864	(0.046)	*0.006*	0.893	(0.039)	*0.009*
Glaucoma	1.210	(0.096)	*0.016*	1.104	(0.068)	*0.108*	1.004	(0.052)	*0.939*

Table A2 (cont.) Cox proportional hazards model estimates for 6-month, 1-year and overal mortality rates, considering surgical delay as a categorical variable—hazard ratio: HR, standard error (se), statistical significance test: *p-value*

Covariates	6-month mortality deaths = 5,093			1-year mortality deaths = 7,321			Overall mortality deaths = 11,916		
Age	1.059	(0.002)	*<0.001*	1.055	(0.002)	*<0.001*	1.045	(0.001)	*<0.001*
Male	1.542	(0.052)	*<0.001*	1.533	(0.043)	*<0.001*	1.438	(0.033)	*<0.001*
Delay >= 3 days	1.199	(0.041)	*<0.001*	1.204	(0.034)	*<0.001*	1.164	(0.025)	*<0.001*
Contract type									
PC	0.801	(0.027)	*<0.001*	0.859	(0.024)	*<0.001*	0.862	(0.020)	*<0.001*
HFP	0.828	(0.030)	*<0.001*	0.901	(0.027)	*<0.001*	0.918	(0.022)	*<0.001*
Provider size									
Medium	1.040	(0.048)	*0.393*	1.039	(0.041)	*0.331*	1.056	(0.032)	*0.077*
Large	0.901	(0.038)	*0.014*	0.947	(0.034)	*0.128*	0.970	(0.027)	*0.270*
Region									
Pampa	0.888	(0.030)	*<0.001*	0.888	(0.025)	*<0.001*	0.850	(0.019)	*<0.001*
Cuyo	1.025	(0.068)	*0.715*	0.966	(0.054)	*0.534*	0.947	(0.041)	*0.201*
NW	0.835	(0.083)	*0.070*	0.780	(0.069)	*0.009*	0.807	(0.056)	*0.002*
NE	0.750	(0.081)	*0.008*	0.683	(0.065)	*<0.001*	0.737	(0.054)	*<0.001*
Patagonia	0.815	(0.130)	*0.197*	0.844	(0.111)	*0.198*	0.809	(0.090)	*0.056*
Rural	0.921	(0.044)	*0.087*	0.956	(0.038)	*0.259*	1.042	(0.032)	*0.182*
Comorbidities									
Arrhytmia	1.110	(0.039)	*0.003*	1.108	(0.033)	*0.001*	1.086	(0.025)	*<0.001*
Atherosclerosis	0.953	(0.039)	*0.237*	1.006	(0.034)	*0.871*	1.023	(0.027)	*0.387*
Ischemic	0.856	(0.026)	*<0.001*	0.895	(0.022)	*<0.001*	0.913	(0.018)	*<0.001*
Insufficiency	1.138	(0.036)	*<0.001*	1.121	(0.029)	*<0.001*	1.170	(0.024)	*<0.001*
Hypertension	0.993	(0.039)	*0.858*	1.013	(0.034)	*0.699*	0.983	(0.026)	*0.524*
Thrombosis	0.723	(0.022)	*<0.001*	0.777	(0.020)	*<0.001*	0.872	(0.017)	*<0.001*
Asthma	0.919	(0.033)	*0.020*	0.898	(0.027)	*<0.001*	0.979	(0.023)	*0.361*
COPD	0.916	(0.048)	*0.098*	0.895	(0.039)	*0.012*	0.916	(0.030)	*0.007*
Alzheimer	0.980	(0.034)	*0.569*	0.986	(0.028)	*0.633*	1.014	(0.022)	*0.517*
Dementia	0.987	(0.033)	*0.701*	1.115	(0.030)	*<0.001*	1.248	(0.026)	*<0.001*
Depression	1.049	(0.035)	*0.146*	1.088	(0.030)	*0.002*	1.096	(0.025)	*<0.001*
Epilepsy	0.925	(0.029)	*0.012*	0.948	(0.025)	*0.039*	0.971	(0.020)	*0.143*
Parkinson	1.174	(0.051)	*<0.001*	1.095	(0.040)	*0.013*	1.114	(0.031)	*<0.001*
Diabetes	1.246	(0.043)	*<0.001*	1.240	(0.035)	*<0.001*	1.195	(0.027)	*<0.001*
Dyslipidemia	0.921	(0.039)	*0.050*	0.883	(0.030)	*<0.001*	0.882	(0.023)	*<0.001*
Hyperthyroidism	1.147	(0.231)	*0.494*	0.878	(0.164)	*0.487*	0.917	(0.122)	*0.516*
Hypothyroidism	0.903	(0.035)	*0.009*	0.894	(0.029)	*0.001*	0.931	(0.023)	*0.003*
Obesity	1.039	(0.180)	*0.827*	1.054	(0.149)	*0.713*	1.022	(0.107)	*0.837*
Arthritis	0.973	(0.032)	*0.407*	0.970	(0.026)	*0.261*	0.982	(0.021)	*0.398*
Arthrosis	0.724	(0.024)	*<0.001*	0.699	(0.019)	*<0.001*	0.718	(0.015)	*<0.001*
Gout	0.990	(0.059)	*0.863*	0.996	(0.049)	*0.931*	1.000	(0.038)	*0.999*
Osteoporosis	0.844	(0.032)	*<0.001*	0.835	(0.026)	*<0.001*	0.851	(0.020)	*<0.001*
Rheumatism	0.905	(0.028)	*0.001*	0.893	(0.023)	*<0.001*	0.926	(0.019)	*<0.001*
Glaucoma	0.965	(0.037)	*0.351*	0.983	(0.031)	*0.598*	0.960	(0.024)	*0.097*