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Research Article

Determinants of Heterogeneity in Management of Patients with AMI Diagnosis: A Retrospective Population Study

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Abstract

Background: In Italy cardiovascular diseases are the leading cause of death. Percutaneous Transluminal Coronary Angioplasty (PTCA) reduces short-term deaths in patients with Acute Myocardial Infarction (AMI). We evaluated inequalities in accessing PTCA among AMI patients.

Methods: This is a retrospective cohort study on 9894 Italian patients hospitalized for AMI in 2003-2007. Generalized linear models were estimated for the probability of PTCA and for time between hospital admission and intervention.

Result: Gender was the most relevant factor in the probability of intervention. Patients ≥75 years and those with higher Charlson index had lower probability. The presence of a coronary unit was associated with greater probability. Surgical intervention within 24 hours from admission was more likely with increasing age and Charlson index and less likely for patients living near a coronary unit. Days between admission and intervention resulted affected by all covariates and deprivation index.

Conclusion: Consistently with literature, we pointed out the role of gender and age on the likelihood of PTCA. Additional factors affecting time to intervention (coronary units and deprivation index) were also identified.

Introduction

In Italy cardiovascular diseases are the leading cause of death [1]. Prevalence [2,3] and mortality rates differ between males and females and among socio-economic statuses [4,5]. Mortality for ischemic heart disease in 2012 was estimated to account for 12% of all the deaths in the population 35-74 years of age, while in the year 2004 there were approximately147.000 cases of infarction. The mortality rates decreased considerably in the last years, from 166x100.000 in men and 43 in women, in 1980, to 64,3 in men and 17,33 in women in 2002 [6].

A procedure that has been shown to reduce overall short-term death of patients who have suffered an Acute Myocardial Infarction (AMI), and to be more effective than the thrombolytic therapy [7], is the Percutaneous Transluminal Coronary Angioplasty (PTCA), a not-invasive procedure that allows to dilate the coronary arteries occluded by atherosclerotic plaques.

The reduction of mortality rates due to the PTCA procedure performed in patients affected by AMI, particularly in the case of ST-segment elevation AMI, has been demonstrated in many studies, but the effectiveness of PTCA on the reduction of mortality depends both on the time to treatment [8,9] and on the experience of the centre [10-12]. Despite the fact that PTCA has been shown to reduce mortality in case of first AMI, not all the patients undergo this procedure [13] and there seems to be substantial heterogeneity in the management of patients with AMI, with inequalities in the access to PTCA.

A number of studies investigated differences related to patient's sex [14,15], assessing a gender bias in favour of men [16,17]. In Finland, disparities between males and females in operation rates were shown in Hetemaa et al. [18], showing a clear difference in revascularisation and angiography rates.

In the region Friuli Venezia Giulia (FVG), located in the North-East of Italy, gender bias was described, by Valent et al. [21], among patients admitted, during the year 2010, in one of the regional Emergency Rooms with chest pain. Waiting time from triage to the visit and electrocardiogram for women was 3 minutes longer than for men. In addition, females admitted to the hospital because of coronary disease had lower likelihood to undergo coronary angioplasty than males.

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In Sweden, Rosvall et al. described also a less frequent adoption of revascularization procedures in patients with low socio-economic status. Moreover, the study assessed similar reduced mortality risk in patients, within different income groups, who underwent the procedure, but differences in long term survival rates after an AMI in patients who did not [19].

In Italy access to PTCA, along with other indicators of efficiency and effectiveness, is monitored in a national project developed by AGENAS (Agenzia Nazionale per I Servizi Sanitari Regionali) called Programma Nazionale Esiti. A set of health outcome indexes for each Italian hospital is calculated and reported on a website (http://95.110.213.190/PNEed14/). This system has been developed to monitor and benchmark the hospital performances. During the year 2013 in Italy the crude proportion of patients with PTCA after a diagnosis of AMI was 39.5% and it has been characterized by an increasing trend in the last 6 years. Socio-economic deprivation of the area of residence [22-24] and ethnicity [25,26] were shown to affect the probability of access to invasive cardiac procedures. However, the Programma Nazionale Esiti cannot take into account the influence of socio-economic factors on the proportion of patients with AMI who undergo PTCA, as information on deprivation cannot be linked to the health data at the individual level in most regions.

Socio-economic deprivation was, however evaluated in a study in the region Tuscany where a lower adoption of the PTCA procedure in patients living in a Health District (HD) with higher deprivation level has been shown by Falcone et al. [20] (OR: 0,71).

In FVG, the addresses of residence of all patients, registered in the Regional Health databases, are georeferenced and this permitted the linkage of each address with a deprivation index estimated at a census block level.

The aim of this study is to assess, in the cohort 2003-2007 of all patients with a diagnosis of the first AMI in Friuli Venezia Giulia (FVG), the presence of inequalities both in the access to PTCA procedures, in short and long term, evaluating the socio-economic status using the deprivation index also. A further goal is to use statistical advanced methods (Zero-inflated Poisson regression) to model and fit the time elapsed between hospital admission and intervention.

Methods

Data sources and enrollment of the cohort

This is a retrospective cohort study based on health administrative databases. The Hospital Discharge Register (HDR) was used to identify the patients hospitalized with a first diagnosis of AMI (ICD-9-CM codes 410*) during the years 2003-2007 in all the regional hospitals. Patients with a previous AMI admission were excluded from the cohort Hospital admissions prior to the date of the first AMI were used to calculate the Charlson index for comorbidity [27-29].

Anonymity of the cohort's patients was guaranteed by the use of an anonymous univocal identification numeric key.

The socio-economic status of the patients was indirectly measured by a deprivation index calculated from data of the 2001 Italian General Census of Population and Housing [30]. In particular, low level of education, unemployment, non-home ownership, one parent family and overcrowding are the five selected variables which represented the multidimensionality of the social and material deprivation index.

This index was, firstly, calculated by summing up the five standardised variables at each census block level, then categorized into five classes: very deprived, deprived, middle, rich and very rich. Since deprivation index data referred to the year 2001 we decided to use the 2007 as last year of observation. In fact, the international economics crisis, begun in 2008, could have modified the deprivation index at the census block level.

The final cohort was derived following four steps:

- 1. The selection of all the regional patients with a diagnosis of AMI (ICD-9-CM codes 410*, years 2003-2007, source HDR): 11.530 cases.
- 2. Identification and exclusion of patients with a previous admission for the same disease (since the year 1995): 830
- 3. Identification and exclusion of patients not residing in region Friuli Venezia Giulia or with missing information on residence at the time of admission: 738.
- 4. Exclusion of patients with a surgery of PTCA or bypass before the date of first admission for AMI: 68.

A cohort of 9894 patients hospitalized with a first diagnosis of AMI between the years 2003 and 2007, residing in FVG and without a previous history of AMI or PTCA, was obtained. Moreover, information on PTCA and Coronary Artery Bypass Grafting (CABG) interventions were derived from the HDR database (respectively ICD-9 codes 360* or 0066* for PTCA and 36* for CABG).

Statistical models

Statistical analyses are based on Generalized Linear Models (GLMs). In particular, we estimated log it models to evaluate the effect of the individual and socio-economic characteristics on the probability to have a surgery event for PTCA or CABG after the first hospital admission for AMI.

Two logistic regression models [31] were considered to evaluate the effect of the individual characteristics on the probability to receive the intervention within 48 hours and a year after the first AMI hospital admission. We included in the model a new variable considering the Health District (HD) of residence, a dummy variable coded 1 if a hospital with a coronary unit is localized in the HD of residence of the patient, 0 otherwise. Then the variables included in the models were: gender, age, class, dummy for the presence of a coronary unit in the health district of residence, class of deprivation index (5 categories, from very poor to very rich), Charslon index.

In addition, for the patients with a surgery event, we analysed the number of days between the admission date for AMI and the first surgical intervention. This outcome is a count random variable which could be modelled through a Poisson regression model. Anyway, the outcome was characterised by an excess of zeros (almost a third of the patients receiving the intervention had the surgery on the same day of admission). It is well known that count data may exhibit overdispersion, which determines the violation of the assumption of an equal conditional mean and variance [32-34]. Excess of zeros is a

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source of over-dispersion that can be treated using alternative models [35,36]. In our study, we used the Zero-Inflated Poisson regression, that is a two-component mixture model combining a point mass at zero with a count distribution, in our case a Poisson distribution. To model the probability of zero vs whichever positive day's count, a binary model was used, with a logit link function [37-39].

Results

Descriptive analysis

Over the 5 year study period, 9894 patients were admitted for AMI. Among these, 4129 were females (41.7%) and 5765 males (58.3%); mean age was 72. The cohort characteristics are shown in Table 1.

The 48% (4783) of the patients had a surgical intervention of PTCA or CABG. Notable differences were found between gender percentages, in fact, while the proportion of men who underwent the surgery was 60%, only the 33% (1392) of the 4129 women had an intervention.

Considering the Health Districts, the patients living in those coded HD1, HD4 and HD6 were more likely to have the surgical intervention.

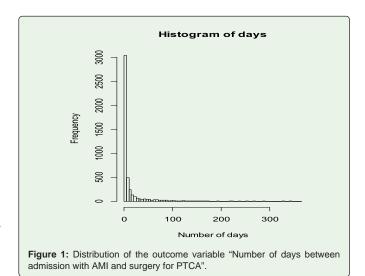
The deprivation index was not available for all the patients, in fact for 849 patients (the 8.5% of the cohort), 366 females and 483 males, this information missed and they were excluded from the relative regression analyses.

Statistical modelling

The result of the logistic regression analysis evaluating the effect of patient's characteristics on the likelihood to receive a surgery event within 48 hours/1 year from the first hospital admission for AMI is reported in Table 2. Patient's gender was the factor with the greatest effect on the probability of surgical intervention. Men had a probability 36% higher than women to access the procedure in 48 hours and even 87% higher considering the long term of one year.

Table 1: Absolute and relative frequencies (by gender, age, HD of residence, deprivation index) of the cohort of patients admitted to hospital with AMI diagnosis and of those who received a surgical intervention for PTCA or CABG.

	Patients with AMI				Patients with surgical					
Variable	hospitalization				intervention (PTCA-CABG)					
	Female		Male		Fem	ale	Male			
	n	%	n	%	n	%	n	%		
Classes of age										
0-55	170	4	847	15	77	6	640	19		
55-64	378	9	1329	23	216	16	1017	30		
65-74	605	19	1566	27	435	32	1091	32		
75-84	1600	39	1515	26	530	39	638	19		
85+	1176	28	508	9	84	6	55	2		
Health district of										
residence										
HD1	904	22	1248	22	298	22	713	21		
HD2	521	13	696	12	151	11	379	11		
HD3	204	5	302	5	68	5	180	5		
HD4	1201	29	1558	27	366	27	933	27		
HD5	450	11	622	11	152	11	362	11		
HD6	849	21	1339	23	307	23	874	25		
Deprivation										
category										
Very deprived	295	8	341	6	103	8	214	7		
Deprived	260	7	312	6	91	7	176	6		
Medium	506	13	646	12	162	13	383	12		
Rich	1087	29	1542	29	344	28	908	29		
Very rich	1615	43	2441	46	538	44	1486	47		



A reduction of the probability of intervention within 48 hours was found when older patients were considered, with almost a geometric decay. In the long term (within 1 year) analysis, instead, the age effects results were partially different.

Compared with patients aged less than 55 years, those in the age class 55-64 had a 18% higher probability of intervention (p-value 0.06), while patients aged 75-84 or 85+ had a reduced probability (OR 0.38 and 0.06, respectively; p-values <0.001). People living in health districts with a coronary unit had a 16% higher probability to access the surgery than the others.

The categories of deprivation index did not significantly pointed out different effects on the probability of surgery. On the other hand, an increase in the Charlson index was significantly associated with a reduction in the probability of intervention.

Figure 1 shows the distribution of the number of days between admission for AMI and the surgery for PTCA. Among the 4783 patients who had at least one PTCA or CABG intervention, 1710 (35%) had surgery on the same day of hospital admission (number of days: 0).

Table 3 shows the results of the Zero-Inflated Poisson regression model. In this model, the canonical link function was the log, then the estimated coefficients showed the effect of each covariate on the logarithm of the average number of days.

The probability of zero days, namely to have the surgical intervention within 24 hours of the admission, decreased with increasing age. All age classes, except those 85+, had a negative effect as compared with patients aged less than 55.

The availability of a coronary unit in the health district of residence had a positive significant effect of being an extra zero (coef. 0,618; p-value <0.01). On the contrary, an increase in the Charlson index corresponded to a reduction of the probability to have the procedure within a day, as shown by the negative effect of the coefficient (coef. -0,04; p-value <0.05).

In the analysis of the Poisson distributed outcome all the variables were significantly related to the mean number of days between the admission and the first procedure of PTCA - CABG. The analysis



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Table 2: Estimation results of the logistic model for the probability of PTCA-CABG procedure within 48 hours and within 1 year from the first hospital admission with AMI diagnosis.

Variable (Intercept)	PTCA within 48h from the hospital admission					PTCA within 1 year from the hospital admission				
	Odds Ratio	Odds Ratio IC (95%)		Pr (> z)		Odds Ratio	Odds Ratio IC (95%)		Pr (> z)	
	0,32	0,24	0,42	1,40e ⁻¹⁵	***	1,27	0,99	1,63	0,0598	
Gender										
Female	1,00					1,00				
Male	1,36	1,20	1,54	1,06e ⁻⁶	***	1,87	1,69	2,07	<2e ⁻¹⁶	***
Classes of age										
<55	1,00					1,00				
55-64	0,78	0,66	0,93	0,005	***	1,18	0,99	1,41	0,063	
65-74	0,60	0,50	0,71	2,62e ⁻⁹	***	0,96	0,81	1,13	0,627	
75-84	0,31	0,25	0,37	<2e ⁻¹⁶	***	0,38	0,32	0,44	<2e ⁻¹⁶	***
85+	0,09	0,07	0,12	<2e ⁻¹⁶	***	0,06	0,05	0,08	<2e ⁻¹⁶	***
Health district of residence										
with CU										
No	1,00					1,00				
Yes	1,85	1,62	2,12	<2e-16	***	1,17	1,05	1,30	0,00386	**
Deprivation index									-	
Very deprived	1,00					1,00				
Deprived	0,89	0,65	1,20	0,43		0,87	0,67	1,13	0,29	
Medium	1,02	0,79	1,31	0,91		0,85	0,68	1,06	0,15	
Rich	0,93	0,75	1,17	0,55		0,87	0,71	1,06	0,156	
Very rich	0,86	0,70	1,08	0,19		0,90	0,74	1,08	0,258	
Charlson index	0,89	0,86	0,92	2,78e ⁻¹²	***	0,90	0,88	0,92	<2e ⁻¹⁶	***

Signif. levels: *** = 0 - ** = 0.01 - * = 0.05 - . = 0.1

showed a significant heterogeneity due to deprivation index classes, despite the results pointed out by the logit model of the first step.

Discussion

Implications of the Study

Our study showed a positive effect of male gender on the mean number of days from admission to surgery. This meant that among patients who did not receive the surgery the same day of admission, females had the procedure earlier than males. We also found a direct relationship between age and the waiting time for the surgery: older patients were admitted to the procedure later than younger ones. An increasing value of the Charlson index showed a positive effect on the expected number of waiting days, this means that patients with serious comorbidities underwent the surgery event generally later than the others. Even if other studies pointed out the association between these factors and the likelihood of undergoing the procedure [18,22,17], this is the first study, to our knowledge, adopting a Zeroinflated Poisson model to fit the time of the intervention also.

Subjects living in "Deprived", "Medium" and "Very rich" areas had surgery earlier than those living in "Very deprived" areas. On the other hand, there was no evidence of association between the deprivation index and the likelihood of undergoing PTCA. Consistently with our result, Falcone et al. [20] found no association between the deprivation index, calculated at a census block level, and access to PTCA in Tuscany, whereas people living in health districts with greater deprivation had lower access to the procedure.

Differently from our results, heterogeneity in the management of coronary heart disease associated with a socio-economic deprivation measure was found in Scotland by MacLeod et al. [22] and in Finland, as shown by Hetemaa et al. [13]. Also in Australia Korda et al. [40] reported not-equity in coronary procedures for patients with ischemic heart disease, probably explained by private health insurance.

Our findings regarding the deprivation index, however, must be interpreted with caution. In fact, the index was not measured at an individual level and some degree of ecologic bias might exist. In addition, despite evidence of its ability to predict general mortality [30], it may not be strictly associated with other health-related measures.

We found significant heterogeneity in the access to PTCA and to CABG procedures within 48 hours and within one year from the first diagnosis of AMI. Gender was the factor, among those analysed, with the greatest influence, but there was also heterogeneity due to age and to the geographical component, which might be related to the presence of a coronary unit nearby.

The gender inequality in a favour of men is consistent with other results in Europe [13,22], in Canada and USA [23, 25] and Australia [40]. On the other hand, the socio-economic status of patients, expressed by the deprivation index, was not associated with the likelihood of having the surgery.

All the variables considered, showed a significant effect on the time span from hospital admission and the surgery procedure. Our results could be taken into consideration to drive a reduction of the inequalities in the access to PTCA and to CABG procedures in Friuli Venezia Giuliaafter a first AMI diagnosis. Our results may indicate that, in addition to the socio-economic level, also the area of residence is a determinant of health inequality.

Patients living in a health district area where there is a hospital with a coronary unit have a higher probability to receive the surgery procedure and earlier than those residing in other areas. Despite our region is relatively small (7.845 km²), this result may suggest that transportation of patients to the coronary units is not always timely.

Improving the emergency system and the timely transportation to the largest hospitals could contribute to reduce inequality.

Limitations

The use of a deprivation index calculated with 2001 census data is a strong limitation because we had to base our cohort on data which are more than 8 years old (2003-2007).



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Table 3: Estimation results of the Zero-inflated Poisson model for the number of days between the first admission with AMI and the surgical intervention for PTCA-CABG.

Variable	Beta	IC 95%		Pr (> z)	
Count model coefficients (poisson with log link)					
(Intercept)	2.898	2.86	2.936	<2e ⁻¹⁶	***
Gender					
Female					
Male	0.193	0.177	0.209	<2e ⁻¹⁶	***
Classes of age					
<55					
55-64	0.375	0.348	0.401	<2e ⁻¹⁶	***
65-74	0.366	0.34	0.391	<2e ⁻¹⁶	***
75-84	0.451	0.424	0.477	<2e ⁻¹⁶	***
85+	0.642	0.596	0.687	<2e ⁻¹⁶	***
Health district of residence with CU					
No					
Yes	-0.02	-0.035	-0.005	0.0099	**
Charlson index	0.03	0.027	0.032	<2e ⁻¹⁶	***
Deprivation index					
Very deprived					
Deprived	-0.121	-0.159	-0.082	7.00E ⁻¹⁰	***
Medium	-0.076	-0.109	-0.043	5.00E ⁻⁰⁶	***
Rich	0.062	0.034	0.09	1.55E ⁻⁰⁵	***
Very rich	-0.029	-0.057	-0.002	0.0342	*
Zero-inflation model coefficients (binomial with logit link)					
(Intercept)	-0.595	-0.787	-0.404	1.08E ⁻⁰⁹	***
Classes of age					
<55					
55-64	-0.384	-0.581	-0.188	0.0001	***
65-74	-0.575	-0.766	-0.384	3.74E ⁻⁰⁹	***
75-84	-0.603	-0.806	-0.401	5.00E ⁻⁰⁹	***
85+	0.005	-0.379	0.388	0.98	
Health district of residence with CU					
No					
Yes	0.618	0.467	0.769	9.00E ⁻¹⁶	***
Charlson index	-0.043	-0.076	-0.01	0.0113	*

Signif. levels: *** = 0 - ** = 0.01 - * = 0.05 - . = 0.1

Our results might not apply to more recent years. However, calculating the crude proportion of patients with AMI in the year 2010 and 2013 (3 and 6 years after the end of the cohort observation) who had a PTCA within one year in our region, we found that, in 2010, 40% of the females with AMI admission had a PTCA procedure (279 out of 694), while the proportion of males was 70% (774 out of 1097). The access proportion increased in both genders as compared with the cohort. 71% of male patients admitted for AMI during the year 2013 had a PTCA (788 out of 1109), and 38% of women (276 out of 721). The differences in these proportions, even if not adjusted, showed that inequality have not decreased in time.

Another limitation of the study is that the deprivation index was calculated at a census block level and not at an individual level, therefore, our results may be affected by an ecological bias.

A proposal for the future is to update these results when more recent socio-economic data will be available.

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