Predictors of In-hospital Mortality in Patients with Acute Limb Ischemia – Lesson Learnt from A Tertiary Hospital in Jakarta

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Research

Abstract

Background

This study aims to identify risk factors associated with in-hospital and 30-days mortality in patients with acute limb ischemia (ALI).

Methods

This study was a single-centered cohort enrolling a total of 160 consecutive patients with a diagnosis of ALI. The ALI diagnosis was based on clinical history, physical examination, and Doppler studies of the extremities. The main outcome of this study is in-hospital and 30-days mortality.

Results

There were a total of 170 patients involving 192 limbs with the diagnosis of ALI. Intra-aortic balloon pump (IABP) insertion (HR 3.4; 95% CI 1.0-11.3, p = 0.042), no vitamin E treatment (HR 5.6; CI 1.7−18.3, 0.004), arrhythmia (HR 12.00; CI 3.8−37.7, p < 0.001), and acute renal failure (HR 6.70; CI 1.88−24.3, p = 0.003) were an independent predictor of intra-hospital mortality. For 30-days mortality, the independent predictors were menopause (HR 3.2; CI 1.16−8.85, p = 0.02); IABP insertion (HR 4.51; CI 1.14−17.92, p = 0.03); arrhythmia (HR 0.11; CI 0.04−0.32, p < 0.001); bleeding requiring transfusion (HR 3.77; CI 0.10-14.28, p = 0.05); and acute renal failure (HR 5.5; CI 1.79−16.95, p = 0.003).

Conclusion

In-hospital mortality in patients with ALI remains high in our center. Several factors contributing to mortality were arrhythmia, renal failure, no vitamin E supplementation, and a history of recent cardiac operation.

Introduction

Acute limb ischemia (ALI) is one of the major vascular emergencies. Acute limb ischemia is defined as a sudden decrease in limb perfusion, threatening the limb's viability.[1] Even though the incidence is not as high as acute coronary syndrome, it potentially causes disability and death if inadequately treated. The incidence of this condition is approximately 1.5 cases per 10,000 persons per year.[2] Thirty-day mortality and amputation rates of ALI are up to 15% and 25%, respectively.[3]

Acute limb ischemia is caused by thrombosis in situ, embolism from the heart or diseased arteries, aortic dissection, and trauma. Clinically, ALI is classified as (I) viable, (II) threatened, and (III) non-viable tissue. This classification helps to guide therapeutic decisions regarding the urgency of intervention, appropriate

pre-intervention evaluation, and intervention modalities.[1,4] The management of ALI aims to restore arterial flow and viability of the limb. Treatment for non-viable ALI is amputation, while the treatment options for viable and threatened ALI involves endovascular or surgical revascularization. Current advances of endovascular therapeutic approach in ALI management have improved overall amputation rates, but mortality rates remain high.[5]

Epidemiological studies on ALI are currently lacking. The incidence and outcome were estimated based on hospital registries, interventional trials, and autopsy studies. Increasing age, level of occlusion, recent myocardial infarction, pre-existing peripheral arterial disease, and cardiopulmonary class are touted to increases morbidity and mortality in patients with ALI.[6] In the modern era of advanced surgical and endovascular revascularization, the prognostic factors may differ from that of prior decades. Factors affecting mortality and morbidity in patients with ALI in the modern era remains inadequately explored. This study aims to identify risk factors associated with in-hospital and 30-days mortality in patients with ALI.

Methods

Study design and data collection

This study was a single-centered cohort enrolling a total of 160 consecutive patients admitted to the National Cardiovascular Center Harapan Kita with a diagnosis of ALI between January 1, 2015 and December 31, 2018. This study is a part of the vascular registry database in the National Cardiovascular Center Harapan Kita which is the national referral center for cardiovascular diseases in Indonesia. The database includes baseline characteristics, diagnosis, comorbidities, procedures performed, and outcome. The ALI diagnosis was based on clinical history, physical examination, and Doppler studies of the extremities. The main outcome of this study is in-hospital and 30-days mortality. All patients were treated based on standard treatment of ALI based on the European Society of Cardiology Guideline on Peripheral Arterial Disease. Additional drugs are left to the discretion of the treating physician. Additional drugs are as follow: Allopurinol 1 × 300 mg, Vitamin E 2 × 400 mg, Pentoxifylline 1200 mg and Sodium bicarbonate 3 × 500 mg. Exclusion criteria were incomplete data (5%). The study has been approved by the institutional review board of the National Cardiovascular Center Harapan Kita

Statistics Analysis

For the baseline characteristics, we classified the patients into survivor and non-survivor; Chi-Square and independent t-test analyses were performed to compare the two groups. We performed a Cox-regression analysis for univariate and multivariate analysis to identify factors associated with in-hospital and 30-days mortality. Variables with p-value < 0.25 in the univariate analysis were included in a multivariate cox-regression analysis to identify the most influential factors related to in-hospital and 30-days mortality. We considered a two-sided p-value of less than 0.05 as statistically significant. All analyses were conducted using SPSS version 23.0.

Results

A total of 170 patients involving 192 limbs were admitted to our hospital with the diagnosis of ALI from January 1st 2015 to December 31st 2018. Ten patients were excluded due to incomplete data. Among 160 patients, 63.1% were male and the mean age was 56 ± 13 years old. In-hospital and 30-days mortality were 28.1% and 36.9%, respectively (Fig. 1). The baseline characteristics of our study population were shown in Table 1. There are no differences between survivor and non-survivor groups in terms of age, gender, onset of ALI, and limb ischemia severity. History of recent operation and aorta involvement were higher in the non-survivor group. Ischemic sign on ECG, low hematocrit, higher creatinine level was more frequent in the non-survivor group. Survival rate was higher in patients receiving Additional treatment such as vitamin E, pentoxifylline, sodium bicarbonate. Complications such as sepsis, acute renal injury, bleeding were more frequent in the non-survivors.

Table 1
Baseline characteristics of population study

Variables	In-hospital Mortality		P value
	Non-survivor (n = 45)	Survivor (n = 115)	
Age (years)	58,9 ± 9,4	55,8 ± 14,3	0,115
Male	28 (62.2%)	73 (63.5%)	1,000
Onset (hours)	52.7 ± 74.7	92.1 ± 111.3	0.041
Involvement of limb	19 (42.2%)	56 (48.7%)	0,705
- Right unilateral	17 (37.8%)	6 (31.3%)	
- Left Unilateral	9 (20%)	23 (20%)	
- Bilateral			
Severity (Rutherford)	8 (17.8%)	24 (20.9%)	0,330
- I	14 (31.1%)	44 (38.3%)	
- IIA	20 (44.4%)	34 (29.6%)	
- IIB	3 (6.7%)	13 (11.3%)	
- III			
Smoker	23 (51.1%)	59 (51.3%)	1.00
Hypertension	29 (64.4%)	66 (57.4%)	0,524
Diabetes Mellitus	14 (31.1%)	35 (30.4%)	0.538
History of coronary artery disease	22 (48.9%)	39 (33.9%)	0,116
History of valvular disease (mitral/aorta)	9 (20%)	13 (11.3%)	0,151
History of recent cardiac operation	15 (33.3%)	15 (13%)	**0,006**
History aortic dissection	3 (30%)	7 (12.3%)	0.163
Etiology thrombosis	23 (51.1%)	75 (65.2%)	0,143
Etiology embolism	19 (42.2%)	32 (27.8%)	0,117
Aortic lesion	2 (4.4%)	0 (0%)	**< 0,001**
Iliac -femoral lesion	26 (57.8%)	62 (53.9%)	0,791
Poplitea-tibial lesion	21 (46.7%)	59 (51.3%)	0,725
Atrial fibrillation	8 (17.8%)	26 (22.6%)	0,648
Ischemic sign on ECG	21 (46.7%)	32 (27.8%)	**0,037**

Variables	In-hospital Mortality		P value
	Non-survivor (n = 45)	Survivor (n = 115)	
Leucocyte > 10.000 /uL	34 (77,3%)	66 (66,7%)	0,281
Hemoglobin < 12 g/dL	22 (48,9%)	36 (32,4%)	0,081
Hematocrit < 34%	24 (53,3%)	82 (75,2%)	**0,013**
Creatinine > 1.2 g/dL	30 (68,2%)	43 (38,7%)	**0,002**
Ejection Fraction on echocardiography (%)	47,6 ± 19,6	50,0 ± 17,8	0,51
TAPSE on echocardiography (cm)	1,9 ± 0,5	2,0 ± 1,5	0,484
Intra Arterial Thrombolytic Therapy (PIAT)	2 (4,4%)	14 (12,2%)	0,239
Surgical Embolectomy	10 (22,2%)	24 (20,9%)	1,000
Heparin treatment	33 (73.3%)	91 (79.1%)	0,563
Pentoxifylline treatment	30 (66.7%)	77 (67,5%)	1
Sodium Bicarbonate treatment	29 (65.9%)	92 (80.7%)	0,049
Vitamin E Treatment	9 (20,0%)	46 (40,7%)	0,023
Allopurinol Treatment	27 (60,0%)	87 (75,7%)	0,049
Aspirin Treatment	16 (37,2%)	58 (51,8%)	0,148
Clopidogrel Treatment	17 (37,8%)	56 (48,7%)	0,285
Statin Therapy	24 (53,3%)	67 (58,8%)	0,655
Septic	14 (31,1%)	8 (7%)	< 0,0001
Arrhythmia	23 (51,1%)	14 (12,2%)	< 0,0001
Bleeding (Gastrointestinal, cerebral)	12 (26,7%)	9 (7,80%)	0,004
Acute Renal Injury	18 (40,0%)	13 (11,3%)	< 0,0001
Duration of hospital stay (days)	11 ± 10	10 ± 8	0.443

Table 2 showed univariate and multivariate analysis of variables related to in-hospital mortality. In the univariate analysis, Intra-Aortic Balloon Pump (IABP) insertion, no treatment of bicarbonate sodium and vitamin E, arrhythmia, bleeding requiring transfusion, and acute renal failure were related to in-hospital mortality. In the multivariate analysis, the predictors for in-hospital mortality were insertion of IABP (HR 3.4; 95% CI 1.0-11.3, p = 0.042); no vitamin E treatment (HR 5.6; CI 1.7−18.3, p = 0.004); arrhythmia (HR 12.00; CI 3.8−37.7, p < 0.001); and acute renal failure (HR 6.70; CI 1.88−24.3, p = 0.003). Bleeding requiring transfusion was not a significant factor.

Table 2
Univariate and multivariate analyses of variables associated with in-hospital mortality

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	0.95 (0.89−1.08)	0.087		
Atrial fibrillation	0.11(0.007−1.743)	0.118		
IABP insertion	25.80 (2.5-244.52)	0.006	3.40 (1.0-11.3)	0.042
History of Aortic dissection	0.079 (0.001−6.866)	0.265		
No Sodium bicarbonate therapy	0.057 (0.005−0.680)	0.023		
No Vitamin E therapy	14.296 (2.004-101.998)	0.008	5.6 (1.7−18.3)	0.004
No Allopurinol therapy	5.58 (0.59−52.36)	0.132		
Sepsis	0.179 (0.02−1.63)	0.127		
Arrhythmia	16.31 (2.52-105.61)	0.003	12.00 (3.8−37.7)	< 0.001
Bleeding requiring transfusion	59.787 (1.19-2991.8)	0.04	3.40 (0.82−14.3)	0.090
Acute renal failure	9.01 (1.11−73.27)	0.04	6.70 (1.88−24.3)	0.003
Leukocyte > 10.000/uL	0.78 (0.16−3.79)	0.756		
Hemoglobin > 12 g/dL	0.38 (0.02−4.92)	0.458		
Creatinine > 1,2 mg/dL	0.43 (0.09-2.00)	0.279		

Table 3 showed the result of univariate and multivariate analysis of variables related to 30-days mortality. In the univariate analysis, risk factors of menopause in women, acute renal failure, arrhythmia, and bleeding requiring transfusion were related to 30-days mortality. In the multivariate analysis, the predictors for 30-days mortality were menopause (HR 3.2; CI 1.16−8.85, p = 0.02); IABP insertion (HR 4.51; CI 1.14−17.92, p = 0.03); arrhythmia (HR 0.11; CI 0.04−0.32, p < 0.001); bleeding requiring transfusion (HR 3.77; CI 0.10-14.28, p = 0.05); and acute renal failure (HR 5.5; CI 1.79−16.95, p = 0.003).

Table 3
Univariate and multivariate analyses of variables associated with 30-days mortality

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Onset	1.00 (0.99−1.01)	0.17		
Rutherford severity	0.36 (0.071−1.88)	0.091		
Menopause	4.17 (1.20-14.46)	0.024	3.20 (1.16−8.85)	0.02
IABP insertion	3.6 (0.78−16.47)	0.099	4.51 (1.14−17.92)	0.03
No vitamin E treatment		0.404		
Acute Renal Failure	4.13 (1.05−16.33)	0.043		
Arrhythmia	0.18 (0.05−0.62)	0.007		
Sepsis	0.179 (0.02−1.63)	0.127		
Arrhythmia	16.31 (2.52-105.61)	0.003	0.11 (0.04−0.32)	< 0.001
Bleeding requiring transfusion	59.787 (1.19-2991.8)	0.04	3.77 (0.10-14.28)	0.05
Acute renal failure	9.01 (1.11−73.27)	0.04	5.50 (1.79−16.95)	0.003
Creatinine > 1,2 mg/dL	0.77 (0.28−2.10)	0.61		

Discussion

Despite recent advances in ALI management, it is still a challenging issue associated with high mortality. The in-hospital mortality rate in our institution was 28.1% in the past 3 years (2015−2018). This number was larger than other studies, which is likely due to the late presentation of patients in our cohort. Clason et al. reported that the 30-days mortality rate among ALI patients was around 26%.[6] Baril et al. showed that the in-hospital mortality for ALI declines from 12.1% in 1998 to 9.0% in 2009 (P < .001) in the United States Medicare population.[5] Endovascular therapy for the treatment of ALI is increasingly used and contributes to mortality reduction in the Medicare population. In our institution, the percentage of patients undergoing endovascular therapy and surgical embolectomy was only 0% and 21.3%, respectively. The remainder of the patients was only managed by anticoagulation without primary reperfusion during hospitalization. The choice of therapeutic modalities was not associated with mortality in our patients. A meta-analysis demonstrated no significant difference in short-term and 12-months mortality, limb amputation, and recurrent ischemia in endovascular or surgical approach in ALI.[7]

There were differences in the subjects' baseline characteristics regarding history of cardiac operation, aortic lesion, and ischemic sign on ECG between survivor and non survivor groups (P-value: 0.006, < 0.001, and 0.037 respectively). These findings describe the degree of atherosclerotic burden and vascular

damage in a patient's body. Patients who presented with any of these history have higher mortality risk. According to several studies, cardiopulmonary complications account for the majority cause of death. Approximately 15 to 20 percent of patients die within one year of presentation of their limb ischemia, usually from the medical illnesses that predispose them to acute limb ischemia.[1,8,9]

Most of the studies reported the risk factors associated with 30-days and 1-year mortality. The data on factors that contribute to in-hospital mortality is currently lacking. This study showed that in-hospital development of cardiac arrhythmias and acute renal failure were associated with mortality. Previously, 30-days mortality and amputation were attributed to several factors, including increasing age, level of occlusion, recent myocardial infarction, pre-existing peripheral arterial disease, and cardiopulmonary functional class.[6] United States Medicare registries indicate that patients with advanced age, chronic renal failure, dementia, cancer, and atrial fibrillation have higher 30-days mortality.[5] In our registry, all of these factors did not contribute to in-hospital mortality.

History of recent cardiac operation is one of the factors contributing to in-hospital mortality. In this registry, 30 from 160 patients had ALI after CABG or valve surgery. Most of these patients have a history of IABP insertion prior to or after the procedure. Approximately 32.6% of patients with ALI who underwent IABP insertion died in-hospital. Allen et al. found that IABP insertion to cardiac surgery patients is a strong risk factor for acute leg ischemia. Morbidity and mortality of ALI after cardiac surgery were 92% and 46%, respectively.[10] Folkert et al. showed that IABP insertion leads to a five-fold increase in ALI.[11] It is interesting to note that vascular complications, including acute limb ischemia remains a significant risk associated with IABP, occurring in 6–25% of cases. IABP insertion could cause leg ischemia from several mechanisms, insertion to femoral branches rather than the common femoral artery could cause limb ischemia, improper insertion/needle puncture, which is too low is the most common cause of ischemic complication during IABP.[12,13]

Lethality in ALI is attributed to the reperfusion injury. After occlusion and tissue ischemia, blood flow restoration may paradoxically exacerbate prior ischemic injury by an overt inflammatory response that promotes local tissue destruction and remote organ dysfunction.[14,15] Reperfusion to severely ischemic muscles may induce the release of toxic metabolites such as potassium, free radicals, and myoglobin, culminating in a life-threatening systemic complications including renal, cardiac and pulmonary failure.[16,17] Reperfusion to rhabdomyolytic muscle induces the release of myoglobin, causing acute tubular necrosis. Reperfusion also induces overflow of intracellular potassium and hydrogen ions due to the destroyed potassium-sodium pump causing metabolic acidosis and cardiac arrhythmia.[16] Acute renal injury and life-threatening arrhythmia are amongst the fatal ALI complications. In our registry, acute renal injury and fatal arrhythmia contributed significantly to in-hospital mortality.

Vitamin E has been known for its antioxidant effect and reducing ischemic reperfusion injury. Vitamin E can inactivate reactive oxygen species (ROS), where its production increased after reperfusion occurred. Reperfusion will increase ROS release, infiltration of inflammatory cells and humoral mediators which

further potentiates cellular damage.[22] Initiation and propagation of ischemic-reperfusion injury depend upon transcription factor activation, which is responsible for the induction of inflammatory genes required for rapid production of some proteins such as cytokine, adhesion molecules, complement factors, and NO synthase.[23,24] Vitamin E also affects the regulator of signal transduction and modification of NF-κB as predominant transcription factor activation during reperfusion.[25] A vitamin E pre-treatment in a model of ischemic-reperfusion of lower limb muscle of patients undergoing aortic cross-clamp during surgical repair of abdominal aortic aneurysm was shown to prevent the accumulation of neutrophils within ischemic and reperfused muscle by reducing expression of endothelial adhesion proteins such as E-selectin and ICAM-1.[26] In patients undergoing aortic aneurysm resection, vitamin E administration was associated with reduced oxidative skeletal muscle damage secondary to ischemia-reperfusion injury.[27]

In our institution, we administered 200 mg of Vitamin E per day in patients with ALI to reduce ischemia-reperfusion injury; however, we cannot provide it for all patients due to insurance reimbursement cap. Surprisingly, our study showed that a no vitamin E treatment in the acute phase of ALI causes a six-fold increased risk for in-hospital mortality. Arato et al. demonstrate that 200 mg vitamin E administration in patients undergoing lower limb vascular surgery, starting from preoperative day until seven days post-operative reduced the level of oxidative stress (lipid peroxidation, antioxidant enzymes) generated after ischemia-reperfusion insult. Vitamin E administration could also reduce white blood cell activation (MPO activation, free-radicals production, expression of adhesion molecules), reverse prooxidant-antioxidant balance and the consecutive local inflammatory process during early reperfusion compare to placebo.[28] To the best of the authors' knowledge, this is the first study to demonstrate the benefit of Vitamin E supplementation in ALI patients. Further randomized controlled trials should be performed to generate more concrete evidence.

In-hospital morbidity of ALI found in our hospital mainly consists of sepsis, arrhythmia (tachy/bradyarrythmia), bleeding (gastrointestinal and cerebral), acute renal injury, and their proportion was significantly higher in non-survivor group. Primary amputation rate during hospitalization is about 20%. We also observed that the number of bleeding correlates with the number sepsis in both survivor and non-survivor groups of in-hospital mortality analysis. Sepsis is one of the most common causes of disseminated intravascular coagulation, which would most likely give way to major bleeding requiring blood transfusion. This explains why bleeding was an independent predictor of mortality in the multivariate analysis for in-hospital and 30-days mortality.[29,30]

Limitation
The registry was single-center, and the data was collected from a National Referral Hospital. There is a potential for selection bias which may explain the high mortality. The data were collected both prospective and retrospectively from medical records. Some of them have incomplete data or were lost to follow up. The treatments were based on physician discretion; nevertheless, it reflects real-world practice.

Conclusion

In-hospital mortality in patients with ALI remains high in our center. Several factors contributing to mortality were arrhythmia, renal failure, no vitamin E supplementation, and a history of recent cardiac operation.

Declarations

Ethics approval and consent to participate

Ethical clearance approved by National Cardiovascular Center Harapan Kita Institutional Review Board.

Consent for publication

All authors read and approved final version of manuscript

Availability of data and materials

Data available upon reasonable request by journal editor

Authors' contributions

Suci Indriani : Conceptualization, Formal Analysis, Writing-Original Draft.

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Tables

Table 1. Baseline characteristics of population study

Variables	In-hospital Mortality		P value
	Non-survivor (n=45)	Survivor (n=115)	
Age (years)	58,9 ± 9,4	55,8 ± 14,3	0,115
Male	28 (62.2%)	73 (63.5%)	1,000
Onset (hours)	52.7±74.7	92.1±111.3	0.041
Involvement of limb			
- Right unilateral	19 (42.2%)	56 (48.7%)	0,705
- Left Unilateral			
- Bilateral	17 (37.8%)	6 (31.3%)	
	9 (20%)	23 (20%)	
Severity (Rutherford)			
- I	8 (17.8%)	24 (20.9%)	0,330
- IIA	14 (31.1%)	44 (38.3%)	
- IIB	20 (44.4%)	34 (29.6%)	
- III	3 (6.7%)	13 (11.3%)	
Smoker	23 (51.1%)	59 (51.3%)	1.00
Hypertension	29 (64.4%)	66 (57.4%)	0,524
Diabetes Mellitus	14 (31.1%)	35 (30.4%)	0.538
History of coronary artery disease	22 (48.9%)	39 (33.9%)	0,116
History of valvular disease (mitral/aorta)	9 (20%)	13 (11.3%)	0,151
History of recent cardiac operation	15 (33.3%)	15 (13%)	**0,006**
History aortic dissection	3 (30 %)	7 (12.3%)	0.163
Etiology thrombosis	23 (51.1%)	75 (65.2%)	0,143

Etiology embolism	19 (42.2%)	32 (27.8%)	0,117
Aortic lesion	2 (4.4%)	0 (0%)	**<0,001**
Iliac -femoral lesion	26 (57.8%)	62 (53.9%)	0,791
Poplitea-tibial lesion	21 (46.7%)	59 (51.3%)	0,725
Atrial fibrillation	8 (17.8%)	26 (22.6%)	0,648
Ischemic sign on ECG	21 (46.7%)	32 (27.8%)	**0,037**
Leucocyte > 10.000 /uL	34 (77,3%)	66 (66,7%)	0,281
Hemoglobin <12 g/dL	22 (48,9%)	36 (32,4%)	0,081
Hematocrit <34%	24 (53,3%)	82 (75,2%)	**0,013**
Creatinine >1.2 g/dL	30 (68,2%)	43 (38,7%)	**0,002**
Ejection Fraction on echocardiography (%)	47,6 ± 19,6	50,0 ± 17,8	0,51
TAPSE on echocardiography (cm)	1,9 ± 0,5	2,0 ± 1,5	0,484
Intra Arterial Thrombolytic Therapy (PIAT)	2 (4,4%)	14 (12,2%)	0,239
Surgical Embolectomy	10 (22,2%)	24 (20,9%)	1,000
Heparin treatment	33 (73.3%)	91 (79.1%)	0,563
Pentoxifylline treatment	30 (66.7%)	77 (67,5%)	1
Sodium Bicarbonate treatment	29 (65.9%)	92 (80.7%)	0,049

Vitamin E Treatment	9 (20,0 %)	46 (40,7 %)	0,023
Allopurinol Treatment	27 (60,0 %)	87 (75,7%)	0,049
Aspirin Treatment	16 (37,2%)	58 (51,8%)	0,148
Clopidogrel Treatment	17 (37,8%)	56 (48,7%)	0,285
Statin Therapy	24 (53,3%)	67 (58,8%)	0,655
Septic	14 (31,1%)	8 (7%)	<0,0001
Arrhythmia	23 (51,1%)	14 (12,2%)	<0,0001
Bleeding (Gastrointestinal, cerebral)	12 (26,7%)	9 (7,80%)	0,004
Acute Renal Injury	18 (40,0%)	13 (11,3%)	<0,0001
Duration of hospital stay (days)	11 ± 10	10 ± 8	0.443

Table 2. Univariate and multivariate analyses of variables associated with in-hospital mortality

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	0.95 (0.89-1.08)	0.087		
Atrial fibrillation	0.11(0.007-1.743)	0.118		
IABP insertion	25.80 (2.5-244.52)	0.006	3.40 (1.0-11.3)	0.042
History of Aortic dissection	0.079 (0.001-6.866)	0.265		
No Sodium bicarbonate therapy	0.057 (0.005-0.680)	0.023		
No Vitamin E therapy	14.296 (2.004-101.998)	0.008	5.6 (1.7-18.3)	0.004
No Allopurinol therapy	5.58 (0.59-52.36)	0.132		
Sepsis	0.179 (0.02-1.63)	0.127		
Arrhythmia	16.31 (2.52-105.61)	0.003	12.00 (3.8-37.7)	<0.001
Bleeding requiring transfusion	59.787 (1.19-2991.8)	0.04	3.40 (0.82-14.3)	0.090
Acute renal failure	9.01 (1.11-73.27)	0.04	6.70 (1.88-24.3)	0.003
Leukocyte > 10.000/uL	0.78 (0.16-3.79)	0.756		
Hemoglobin >12 g/dL	0.38 (0.02-4.92)	0.458		
Creatinine >1,2 mg/dL	0.43 (0.09-2.00)	0.279		

Table 3. Univariate and multivariate analyses of variables associated with 30-days mortality

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Onset	1.00 (0.99-1.01)	0.17		
Rutherford severity	0.36 (0.071-1.88)	0.091		
Menopause	4.17 (1.20-14.46)	0.024	3.20 (1.16-8.85)	0.02
IABP insertion	3.6 (0.78-16.47)	0.099	4.51 (1.14-17.92)	0.03
No vitamin E treatment		0.404		
Acute Renal Failure	4.13 (1.05-16.33)	0.043		
Arrhythmia	0.18 (0.05 – 0.62)	0.007		
Sepsis	0.179 (0.02-1.63)	0.127		
Arrhythmia	16.31 (2.52-105.61)	0.003	0.11 (0.04-0.32)	<0.001
Bleeding requiring transfusion	59.787 (1.19-2991.8)	0.04	3.77 (0.10-14.28)	0.05
Acute renal failure	9.01 (1.11-73.27)	0.04	5.50 (1.79-16.95)	0.003
Creatinine >1,2 mg/dL	0.77 (0.28-2.10)	0.61		

Figures
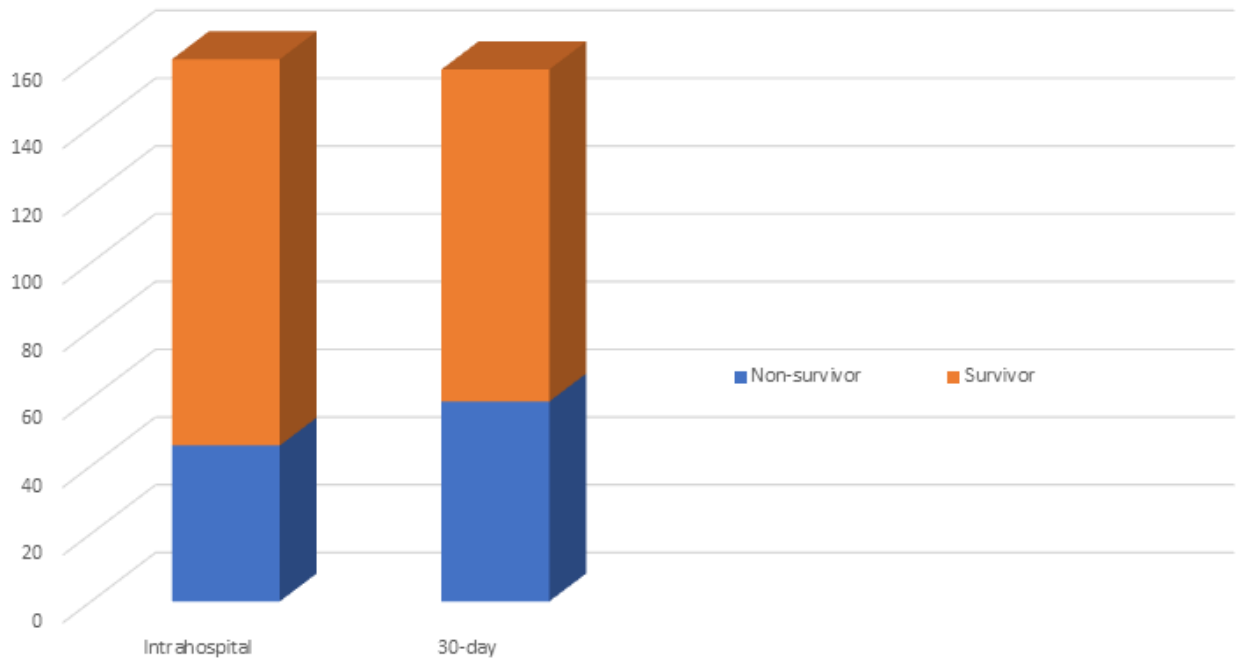
Figure 1

In-hospital and 30-days mortality