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Isolated cardiac troponin rise does not modify the prognosis in elderly patients with hip fracture

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Abstract

Perioperative myocardial infarction remains a life-threatening complication in noncardiac surgery and even an isolated troponin rise (ITR) is associated with significant mortality. Our aim was to assess the prognostic value of ITR in elderly patients with hip fracture.

In this cohort study, all patients admitted between 2009 and 2013 in our dedicated geriatric postoperative unit after hip fracture surgery with a cardiac troponin I determination were included and divided into Control, ITR, and acute coronary syndrome (ACS) groups. The primary end point was a composite criteria defined as 6-month mortality and/or re-hospitalization. Secondary end points included 30-day mortality, 6-month mortality, and 6-month functional outcome.

Three hundred twelve patients were (age 85 ± 7 years) divided into Control (n = 217), ITR (n = 50), and ACS (n = 45) groups. There was no significant difference for any postoperative complications between ITR and Control groups. In contrast, atrial fibrillation, acute heart failure, hemorrhage, and ICU admission were significantly more frequent in the ACS group. Compared to the Control group, 6-month mortality and/or rehospitalization was not significantly modified in the ITR group (26% vs. 28%, $P = 0.84$, 95% confidence interval [CI] of the difference -13%–14%), whereas it was increased in the ACS group (44% vs. 28%, $P = 0.02$, 95% CI of the difference 2%–32%). ITR was not associated with a higher risk of new institutionalization or impaired walking ability at 6 months, in contrast to ACS group.

In elderly patients with hip fracture, ITR was not associated with a significant increase in death and/or rehospitalization within 6 months.

Abbreviations: ACS = acute coronary syndrome, ADL = Activities of Daily Living, CI = Confidence Interval, CIRS = Cumulative Illness Rating scale, CNIL = French National Commission on Computing and Liberty, CPP = ethics committee, cTn = cardiac troponin, ECG = electrocardiogram, IADL = Instrumental Activities of Daily Living, ICU = intensive care unit, ITR = isolated troponin rise, STEMI = ST-elevation myocardial infarction, UPOG = Unit for Peri-Operative Geriatric care.

Keywords: biomarkers, elderly, hip fracture, prognosis, troponin I

1. Introduction

Perioperative myocardial infarction remains a frequent and life-threatening complication in noncardiac surgery.[1–3] In 2012, redefinition of acute myocardial infarction highlighted the importance of troponin elevation in association with either electrocardiographic changes, and/or clinical symptoms of ischemia, and/or new wall motion anomalies.[4] However, large database analyses have recently extended the concept of perioperative myocardial infarction to myocardial injury after noncardiac surgery because even subtle and isolated increase in troponin irrespective of ischemic features (i.e., ischemic symptoms and electrocardiogram [ECG] findings) is associated with a significant mortality risk.[5,6] This result is in agreement with previous studies showing that isolated troponin rise (ITR) is associated with an increased mortality risk in various non-ischemic conditions such as sepsis,[7] pulmonary embolism,[8] renal failure,[9] and acute respiratory failure in chronic obstructive pulmonary disease patient.[10]

Hip fracture is a frequent emergency condition in the geriatric population, associated with a poor prognosis[11,12] and with a 5- to 8-fold increased mortality risk in the first 6 months following hip fracture surgery.[13] Mortality rate at 6 months varies across studies between 19% and 25%.[14,15] The prognostic significance of a cardiac troponin rise remains controversial in elderly patients with hip fracture. Some studies reported an increase in short- and

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long-term mortality,[16–18] whereas other did not.[19–21] Moreover, these studies did not distinguish ITR and myocardial infarction according to its universal definition.[4] In these elderly patients with hip fracture, an ITR may occur more frequently because of events such as atrial fibrillation or transient supply/demand mismatch. Moreover, the mortality risk related to nonischemic causes is higher and remains markedly increased over a longer perioperative period in these elderly patients,[22] which may be greater than the risk associated with myocardial injury itself. Therefore, there is a knowledge gap concerning the prognostic role of postoperative troponin in elderly patients with hip fracture and results obtained in younger patients who undergo scheduled surgery may or may not apply to this frail population.[23]

The aim of our study was to assess the prognostic value of ITR in elderly patients with hip fracture. We tested the hypothesis that ITR increases the rate of death and/or rehospitalization within 6 months after hip fracture. We also assessed other clinically important prognostic variables in this elderly population such as functional status, walking ability, and autonomy.

2. Material and methods

This study was approved by the ethics committee (CPP Pitié-Salpêtrière, Paris, France) and as the study was observational, informed consent was waived. Nevertheless, all patients were informed about their inclusion in the database and had the option to refuse it. The database was declared to the French National Commission on Computing and Liberty (CNIL, Paris, France). This study was carried out in our 10-bed perioperative geriatric unit (Unit for Peri-Operative Geriatric care, UPOG) in a tertiary university teaching hospital.

The database was created in June 2009 and acquisition of data was prospective. Nevertheless, this study should be considered as retrospective since the design of this study was performed later. The statistical plan of the study was decided before the statistical analysis, except the sensitivity analysis using multivariable matching (*vide infra*). A significant proportion of these patients (n = 203) has been included in a previous study.[24]

2.1. Patients

From June 2009 to June 2013, all consecutive patients admitted to our UPOG were evaluated for eligibility. Detailed methodology has been previously reported.[24] Patients were included if they were 70 years of age or older (requirement to be admitted in the UPOG) and if their primary presentation was due to hip fracture, and if they had a postoperative cardiac troponin measurement. Patients were excluded if they presented with multiple or metastatic fractures, a redo surgery, if they were already hospitalized at the time of diagnosis, and if there was no troponin measurement. We stopped recruiting patients in June 2013 for that study when ultrasensitive troponin measurement was implemented in our institution to ensure that the same method of measurement was used.

2.2. Data collection

Prospectively collected data included age, sex, living conditions, walking ability, functional autonomy, medical history, medications, type of fracture and surgical treatment, type of anesthesia (general vs locoregional), and any nerve block provided for analgesia. Associated comorbidities were assessed using the Cumulative Illness Rating scale (CIRS).[25] Functional status was evaluated with the Activities of Daily Living (ADL) scale[26] and the Instrumental Activities of Daily Living (IADL) scale.[27] We recorded hemoglobin level during the acute care period, serum creatinine, and estimated creatinine clearance using the Cockroft formula.[28] Chronic renal failure was defined as an estimated creatinine clearance $\leq$60 mL/min.

Considering silent myocardial infarction,[4,29] ECG and cardiac troponin I (cTnI) measurement were routinely performed within the first 3 days after surgery in all patients. cTnI measurement at admission in the emergency department (preoperative value) relied on the emergency physician decision. A 12-lead ECG was routinely performed at the admission into the emergency department, at admission into the geriatric unit, and in presence of any evocating clinical symptoms. ECGs were all reviewed by an expert panel unaware of the troponin level, including 2 independent physicians, specialized in geriatrics and cardiology (H.V., A.B, J.C.B, J.B.) as previously described.[30] The percentage of agreement between experts was 97% (kappa score = 0.94, 95% confidence interval [CI] 0.85–0.99). A cTnI rise was defined in presence of a value $>$0.05 ng/L (Dimension Xpand analyser, Siemens Healthcare Diagnostics France, Saint-Denis, France). Undetectable values were quoted as 0.05 ng/L. An acute coronary syndrome (ACS) was defined following the third universal definition of myocardial infarction:[4] cTnI rises with at least 1 value above the 99th percentile upper reference limit and with at least new significant ST-segment-T wave changes, new left bundle branch block, development of pathological Q waves in the ECG, or new wall motion anomalies. Patients were regrouped according to troponin level and ECG interpretation, as Control group (no significant ECG change and no troponin rise), ITR Group (troponin rise without significant ECG changes), and the ACS group (troponin rise with significant ECG changes).

2.3. Outcomes and follow-up

All complications during the acute care period were recorded including delirium, stool impaction, urinary retention requiring drainage, pain, pressure ulcer, infection, thromboembolic event, postoperative anemia and transfusion, swallowing disorders, acute cardiac failure, atrial fibrillation, stroke and admission into intensive care unit (ICU), as previously described.[24] Patients requiring coronary angiography and cardiologic transfer were considered as ICU transfers. We also recorded therapeutic intensification (i.e., new administration of antiaggregants, statin, converting enzyme inhibitor, or beta-blockers, or coronary stenting or coronary artery bypass) as previously described.[31]

Patients were followed until death or 6 months after admission for living status and functional outcome (ability to walk, ADL, and IADL scores). Surviving patients or their relatives were contacted and interviewed by telephone. For rehospitalization, day-case admissions for chemotherapy, hemodialysis, pacemaker replacement, and geriatric assessment were not considered as hospitalization. For any new institutionalization at 6 months, patients who were dead were censored and patients who were already institutionalized before hip fracture were excluded.

2.4. End points

The primary end point was a composite criteria defined as 6-month mortality and/or rehospitalization from any cause. Secondary end points included acute care and/or rehabilitation mortality, 30-day mortality, 6-month mortality, 6-month

functional outcome (ability to walk, ADL, and IADL), and new institutionalization.

2.5. Statistical analysis

The sample size was based on all available patients and thus no a priori power calculation was conducted. Data are expressed as mean ± SD or median (25th–75th interquartile) for non-Gaussian variables, and number (percentages). Comparison between groups was performed using analysis of variance and the Newman-Keuls test, the multiple comparison Kruskall-Wallis test, and Fisher exact method with Bonferroni correction, when appropriate. Survival was estimated using the Kaplan-Meier method and comparisons were performed using the log-rank test. The Cox proportional hazards model was used to determine the predictors of death and rehospitalization at 6 months, death at 6 months, and new institutionalization at 6 months. Only variables known to be previously associated with the prognosis (age, sex, CIRS)[24] were entered into the Cox model and we added the group (control, ITR, and ACS). We calculated the risk ratio and its 95% CI in association with these variables. We performed a sensitivity analysis (post hoc test) and also conducted a multivariable matching aiming to create two groups of patients with similar preoperative characteristics (i.e., age, sex, and CIRS 52), one with postoperative ITR and the other group without any troponin elevation. Matched populations consisted of 50 patients with ITR and 100 control patients. Using conditional logistic regression and double robust estimator, we then estimated the impact of ITR on study primary outcome, that is, 6-month mortality and/or rehospitalization.

Statistical analysis was performed using NCSS 7.0 software (Statistical solutions Ltd., Cork, Ireland). All *P* values were 2-tailed and *P* values of <0.05 were considered significant.

3. Results

During the study period, 365 patients with a hip fracture were admitted. Of these, 53 were excluded because of pathological fracture (n = 3), redo surgery (n = 7), preexisting hospitalization (n = 4), and absence of cTnI measurement (n = 39); therefore, 312 (85%) were finally retained in the analysis (Fig. 1). Postoperative rise in cTnI occurred in 94 (30%) patients and ACS was diagnosed in 45 (14%) patients (Table 1). Nine ACS were ST-elevation myocardial infarction (STEMI) and 36 were non-STEMI. Thus, patients were divided in Control group (n = 217), ITR group (n = 50), and ACS group (n = 45) (Fig. 1). The main characteristics of the patients are presented in Table 1. Preoperative cTnI was available in only 65 patients and was elevated in only 13 patients (0.30 [0.16–1.11] ng/L). Six of these patients belong to the ITR group and 7 to the ACS group. Median maximum postoperative cTnI values were 0.05 (0.05–0.05) ng/L in Control group, 0.11 (0.08–0.23) ng/L in ITR group, and 0.60 (0.15–1.76) ng/L in ACS group. ECG modifications that did not meet the ACS criteria were observed in 70 (32%) patients in the control group.

Comorbidities were similar between ITR and Control groups, except for creatinine clearance, type of fracture and surgery, and IADL score. Coronary artery disease, heart failure, and low creatinine clearance were more frequent in the ACS group than in the Control group. There was no significant difference between ITR and ACS groups (Table 1). Most patients underwent general anesthesia and half of them benefited from regional nerve block for analgesia, without significant differences between groups (Table 1).

3.1. Short-term outcome

Table 2 shows the therapeutic intensification administered in the 3 groups. Patients in the ACS group received more frequently new antiaggregants, statins, and beta-blockers. Coronary angiography was performed in only 6 patients, all in the ACS group, showing coronary stenosis in 4 patients and coronary occlusion in 3 patients, one of them had a coronary stent. Tako-tsubo syndrome was diagnosed in 1 patient. Echocardiography was performed in 81 (26%) patients, but we did not observe significant changes between the 3 groups. Ejection fraction was 54% ± 21% (n = 48), 53% ± 20% (n = 17), and 43% ± 25% (n = 16), in control, ITR, and ACS groups, respectively, without significant difference between groups ($P = 0.24$).

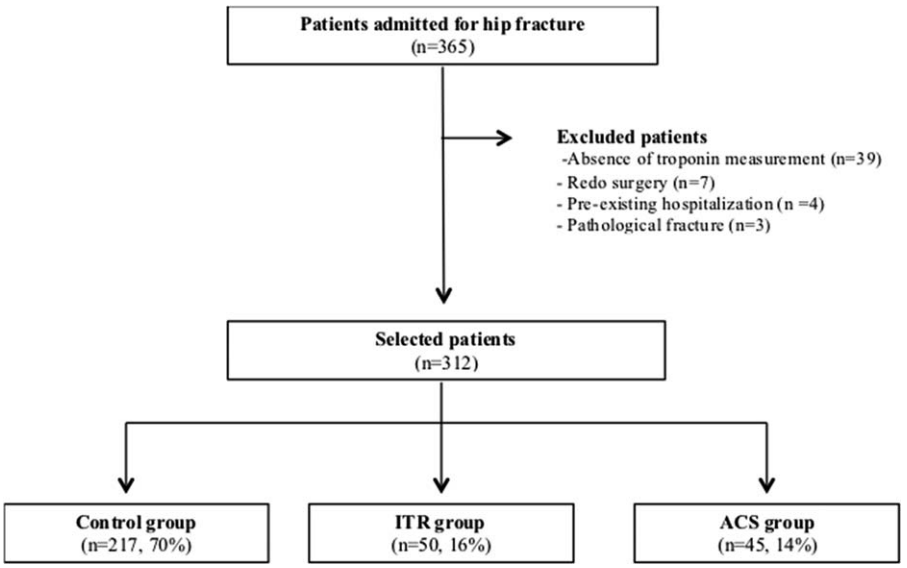

Figure 1. Study flow chart. ACS = acute coronary syndrome, ITR = isolated troponin rise.

Table 1

Main characteristics of the three groups.

	Control (n = 217)	Isolated troponin rise (n = 50)	Acute coronary syndrome (n = 45)	*P*
Age, y	86 ± 7	87 ± 6	84 ± 9	0.09
Men	58 (27)	11 (22)	14 (32)	0.60
Medical history				
Dementia	91 (42)	22 (44)	16 (36)	0.67
Hypertension	134 (62)	35 (70)	35 (78)	0.09
Diabetes	29 (13)	5 (10)	10 (22)	0.20
Atrial fibrillation	50 (23)	12 (24)	14 (31)	0.52
Coronary artery disease	35 (16)	12 (24)	15 (33)*	0.02
Cardiac failure	31 (14)	12 (24)	14 (31)*	0.01
Stroke	33 (15)	12 (24)	9 (20)	0.29
Heart valve disease	14 (6)	4 (8)	5 (11)	0.54
COPD	22 (10)	2 (4)	3 (7)	0.33
Chronic renal failure	76 (35)	20 (40)	17 (38)	0.78
Estimated creatinine clearance, mL/min	56 ± 24	44 ± 21*	46 ± 19*,†	<0.001
Estimated creatinine clearance <30 mL/min	21 (10)	15 (30)*	10 (22)*	<0.001
Cancer	44 (20)	12 (24)	11 (24)	0.74
ASA Score				
1	7 (3)	2 (4)	0 (0)	
2	78 (36)	16 (22)	12 (27)	0.28
3	94 (43)	28 (56)	23 (51)	
4	38 (17)	4 (8)	10 (22)	
CIRS 52	8 (6–11)	8 (7–12)	10 (7–13)	0.07
Charlson score	2 (1–3)	3 (1–4)	2 (1–4)	0.06
Pre-operative hemoglobin, g/dL	12.2 ± 1.5	12.1 ± 1.6	12.2 ± 1.3	0.91
Pre-operative anemia	96 (45)	24 (48)	23 (51)	0.70
Autonomy				
ADL	5 (3–6)	5 (2–6)	5 (4–6)	0.09
IADL	2 (1–4)	1 (0–3)*	2 (1–4)	0.02
Medication				
Anticoagulant	27 (12)	7 (14)	9 (20)	0.41
Antiaggregants	88 (41)	16 (32)	20 (44)	0.42
Amiodarone	23 (11)	5 (10)	10 (22)	0.08
Digoxine	8 (4)	0 (0)	1 (2)	0.36
Beta-blockers	53 (24)	18 (36)	11 (24)	0.23
CEI/sartan	87 (40)	22 (44)	21 (47)	0.67
Statin	48 (22)	14 (28)	11 (24)	0.66
Calcium inhibitor	55 (25)	12 (24)	10 (22)	0.90
Nitrate	12 (5)	4 (8)	6 (13)	0.17
Diuretic	44 (20)	17 (34)	18 (40)*	0.006
Walking ability				
No walking disability	125 (58)	26 (52)	15 (33)*	0.01
Moderate walking disability	89 (41)	22 (44)	28 (64)*	0.03
Does not walk	3 (1)	2 (4)	2 (4)	0.30
Fracture				
Intertrochanteric fracture	124 (57)	17 (34)*	27 (40)	0.008
Femoral neck fracture	93 (43)	33 (66)*	18 (60)	
Anesthesia				
General anesthesia	172 (95)	32 (100)	36 (95)	0.43
Locoregional anesthesia	9 (5)	0 (0)	2 (5)	
Missing values	36	18	7	
Nerve block for analgesia	85 (47)	21 (66)	17 (45)	0.13
Missing values	36	18	7	
Surgery				
Gamma nail	116 (53)	14 (28)*	27 (60)†	0.002
Dynamic hip screw	26 (12)	5 (10)	3 (7)	0.57
Unipolar prosthesis	68 (31)	28 (56)*	13 (29)†	0.003
Bipolar prosthesis	7 (3)	3 (6)	2 (4)	0.64

Data are mean ± DS, median (25th–75th interquartile), or number (percentage). ADL = activities of daily living scale, ASA = American Society of Anesthesiology, CEI = converting enzyme inhibitors, CIRS 52 = cumulative illness rating scale, COPD = chronic obstructive pulmonary disease, IADL = instrumental activities of daily living activities.

* $P < 0.05$ vs. control.

† $P < 0.05$ vs. isolated troponin rise.

Table 2

Therapeutic intensification in the 3 groups.

	Control (n = 217)	Isolated troponin rise (n = 50)	Acute coronary syndrome (n = 45)	P
Antiaggregants	11 (5)	5 (10)*	13 (29)*,†	<0.001
Statin	10 (5)	9 (18)*	14 (31)*,†	<0.001
CEI	3 (1)	0 (0)	2 (4)	0.20
Beta-blockers	7 (3)	4 (8)*	8 (18)*,†	<0.001
Any of these drugs	24 (11)	11 (22)	23 (51)*,†	<0.001
Coronary stent	0 (0)	0 (0)	1 (2)	0.05

Data are number (percentage). ADL = activities of daily living scale, CEI = converting enzyme inhibitors, CIRS 52 = cumulative illness rating scale, COPD = chronic obstructive pulmonary disease, IADL = instrumental activities of daily living activities.

* $P < 0.05$ vs. control.

† $P < 0.05$ vs. isolated troponin rise.

The main complications during hospital and rehabilitation stay until home return are presented in Table 3. There was no significant difference for any outcomes between the ITR and Control groups. In contrast, atrial fibrillation, acute heart failure, stroke, infections, hemorrhage, ICU admission, acute care, and/or rehabilitation mortality were significantly more frequent in the ACS group compared with the Control group. Fewer patients were able to return at home in the ACS group than in the Control group.

Table 3

Acute care, rehabilitation, and autonomy at 6 months.

	Control (n = 217)	Isolated troponin rise (n = 50)	Acute coronary syndrome (n = 45)	P
Acute care complications				
Denutrition*	206 (96)	47 (94)	42 (98)	0.68
Delirium	81 (37)	22 (44)	20 (45)	0.52
Pain	194 (89)	48 (96)	44 (98)	0.09
Swallowing disorders	76 (35)	21 (42)	19 (42)	0.49
Urinary retention	57 (26)	17 (34)	16 (36)	0.31
Stool impaction	92 (42)	18 (36)	25 (56)	0.14
Pressure ulcer	22 (10)	5 (10)	2 (4)	0.48
Atrial fibrillation	14 (6)	5 (10)	10 (22)†	0.004
Acute cardiac failure	28 (13)	7 (14)	15 (33)†	0.002
Stroke	0 (0)	1 (2)	3 (7)†	0.001
Infection	42 (19)	16 (32)	16 (36)	0.02
Venous thromboembolism	12 (5)	2 (4)	5 (11)	0.29
Hemorrhage	27 (12)	2 (4)	10 (22)‡	0.03
Post-operative anemia	21é (98)	48 (96)	43 (96)	0.65
Blood transfusion	127 (58)	28 (56)	33 (73)	0.14
Admission into ICU	5 (2)	3 (6)	7 (16)†	<0.001
LOS acute care, days	10 (8–14)	10 (8–14)	15 (10–23)†,‡	<0.001
Admission to rehabilitation care	176 (81)	39 (78)	36 (80)	0.88
LOS rehabilitation care, days	41 (27–57)	38 (22–53)	37 (19–77)	0.74
Total LOS (acute and rehabilitation care), days	44 (23–63)	42 (22–61)	43 (24–85)	0.45
Death during acute care	7 (3)	1 (2)	4 (9)	0.15
Death during rehabilitation care	10 (6)	5 (13)	6 (17)	0.06
Death during acute care and/or rehabilitation	17 (8)	6 (12)	10 (22)†	0.02
New admission into nursing home	20 (9)	8 (16)	9 (20)	0.08
Return to home§	180 (83)	36 (72)	25 (27)†	<0.001
At 30 days	(n = 210)	(n = 19)	(n = 41)	
Readmission within 30 days	11 (5)	0 (0)	7 (17)‡	0.002
Redo surgery within 30 days	3 (1)	1 (2)	1 (2)	0.89
At 6 mo				
Walking ability	(n = 179)	(n = 42)	(n = 32)	
No walking disability	55 (31)	13 (31)	9 (27)	0.03
Moderate walking disability	113 (63)	23 (46)	18 (55)	0.51
Does not walk	11 (63)	6 (14)	6 (60)	0.95
Autonomy	(n = 159)	(n = 38)	(n = 31)	
ADL	5 (2–6)	3 (2–5)	3 (1–5)†	0.03
IADL	2 (0–4)	1 (0–3)	1 (1–3)	0.38

Data are mean ± DS, median (25–75 interquartile), or number (percentage). ADL = activities of daily living scale, CIRS 52 = cumulative illness rating scale, IADL = instrumental activities of daily living scale, ICU = intensive care unit, LOS = length of stay, LOS = length of stay.

* 4 missing values, 2 in Control group and 2 in acute coronary syndrome group.

† $P < 0.05$ vs control.

‡ $P < 0.05$ vs. troponin rise group.

§ 1: missing value in Control group. #: patients previously living in an institution were considered as returning to home.

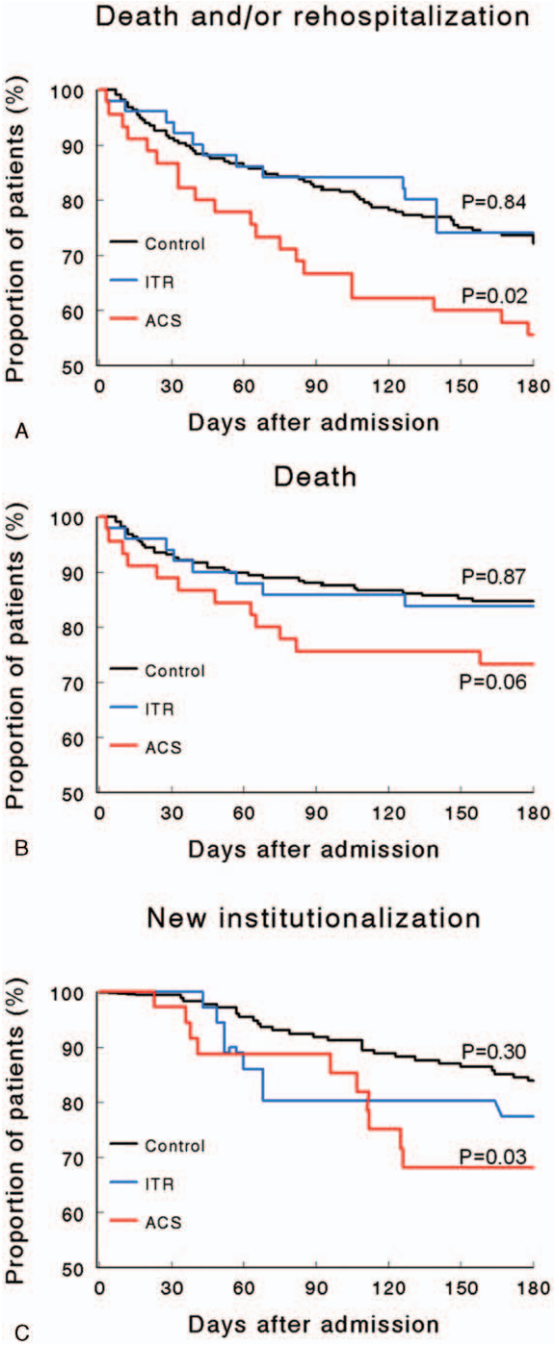

Figure 2. Nonadjusted survival curves for death and/or rehospitalization (primary endpoint, Panel A), death (Panel B), and new institutionalization (Panel C) in Control group (n=217), isolated troponin rise (ITR, n=50) group, and acute coronary syndrome (ACS, n=45) group. For new institutionalization, death was considered as a censored observation and patients who were previously in an institution were excluded. *P* values refer to log-rank test.

3.2. Long-term outcome

Only 2 patients were lost on follow-up. Among the 310 patients with complete follow-up, death occurred in 53 (17%) patients and rehospitalization occurred in 45 (15%) patients, and 93 (30%) patients fulfilled the primary endpoint (death and/or rehospitalization). Death occurred in 5 (11%) patients who were rehospitalized. The main causes of rehospitalization were medical issues (n=23), falls (n=12) with refracture (n=10), postoperative infection (n=4), postoperative mechanical complication (n=1), and nonorthopedic surgery (n=3). Compared to the Control group, 6-month mortality and/or rehospitalization was not significantly modified in the ITR group (26% vs. 27%, $P=0.84$; 95% CI of the difference −10 to 17%), whereas it was greater in the ACS group (44% vs. 27%, $P=0.02$, 95% CI of the difference 2%–32%) (Fig. 2). Similarly, there was no significant difference between the ITR group and the Control group for 6-month death and new institutionalization. In contrast, the risk of new institutionalization was significantly increased in the ACS group compared with the Control group (Fig. 2). In the multivariable cox proportional-hazards analysis, when taken in consideration variables known to impact the long-term outcomes (age, sex, and CIRS 52), ITR was not associated with a higher risk of death and/or rehospitalization, death, or new institutionalization. In contrast, the risks of death and/or rehospitalization and new institutionalization were significantly increased in the ACS group compared with Control group (Table 4). We also conducted a multivariate matching aiming to create 2 groups of patients with similar preoperative characteristics (i.e., age, sex, and CIRS 52), but one with postoperative ITR (n=50) and the other group (n=100) without any troponin elevation. Within this matched population, the odds ratio associated with postoperative ITR to predict 6-month mortality and/or rehospitalization was 1.04 (95% CI 0.50–2.13; $P=0.92$). This result was consistent with that obtained with direct regression approach and suggests that postoperative ITR after hip fracture surgery is not associated with worse long-term outcome.

There was no significant difference for the 6-month ability to walk, ADL, and IADL scores between the ITR and Control groups. In contrast, autonomy of patients in ACS group was lower than patients in Control group, as they were less able to walk and ADL score was lower (Table 3).

4. Discussion

In this study, we found that ITR was not predictive of death and/or rehospitalization during the 6-month period following hip fracture in elderly patients. In addition, ITR did not significantly influence any other outcomes including postoperative complications, in-hospital stay, admission to ICU, new institutionalization, walking ability, and functional status. By contrast, a cTnI rise within the context of ACS was associated with a significant increase in death and/or rehospitalization within 6 months, and a poorer outcome considering admission to ICU, new institutionalization, walking inability, and functional status.

The prognostic significance of troponin rise remains controversial in elderly patients with hip fracture. A few studies have suggested that a troponin rise is not associated with intrahospital mortality.[19] In contrast, Dawson-Bowling et al[18] reported an association with intrahospital mortality, Talsnes et al[17] with 3-month mortality, and Chong et al[16] with 1-year mortality. More recently, Hietala et al[32] also reported an association between cTnT rise and 30-day and 1-year mortality. However, this association should be carefully analyzed, considering 3 points. First, these studies did not delineate ITR and ACS, although ACS is known to be associated with its own mortality risk, particularly in elderly patients.[33] Second, most of these studies did not provide detailed information concerning comorbidities. Lastly, other important long-term outcome variables, known to be clinically important in the elderly population, were not considered. Taken altogether, ECG findings and comorbidities could play an important part in the association between ITR and outcome.

Table 4

Multivariable analysis predicting death, death, and/or rehospitalization (primary end point), and new institutionalization.

Variables	Risk ratio (95% CI)	*P*
Prediction of death (n = 312)		
Age	1.04 (0.99–1.08)	0.10
Male sex	1.72 (0.93–3.19)	0.08
CIRS 52	1.13 (1.06–1.20)	0.001
Control group	1	—
Isolated troponin rise group	0.93 (0.43–2.04)	0.86
Acute coronary syndrome group	1.72 (0.93–3.19)	0.13
Prediction of death and/or rehospitalization (n = 312)		
Age	1.01 (0.98–1.05)	0.40
Male sex	1.14 (0.70–1.84)	0.60
CIRS 52	1.13 (1.07–1.18)	<0.001
Control group	1	—
Isolated troponin rise group	0.84 (0.46–1.55)	0.59
Acute coronary syndrome group	1.67 (1.00–2.77)	0.048
Prediction of new institutionalization (n = 274)*		
Age	1.10 (1.05–1.15)	<0.001
Male sex	1.02 (0.48–2.17)	0.95
CIRS 52	1.05 (0.96–1.13)	0.28
Control group	1	—
Isolated troponin rise group	1.44 (0.65–3.18)	0.36
Acute coronary syndrome group	2.18 (1.05–4.52)	0.04

CI = confidence interval, CIRS = cumulative illness rating scale.

* Only patients who were not previously living in an institution were considered and patients who died were censored.

Our results contrast with those of a recent large study (n = 15,065) of patients aged 45 years or older undergoing noncardiac surgery with postoperative cTnT measurement.[6] In this study, an ITR, irrespective of the presence of an ischemic ECG feature, independently predicted 30-day mortality. Van Weas et al[34] also reported that increase in postoperative troponin was associated to an increase in 30-day mortality in patients over 60 years undergoing scheduled noncardiac surgery. However, van Waes et al[34] did not separate patients with ITR and those with ACS. But our results are in agreement with those reported by Huddleston et al[35] in elderly patients with hip fracture who classified patients as clinically verified myocardial infarction (equivalent to ACS), subclinical myocardial ischemia (isolated elevation of troponin or CK-MB), or no myocardial ischemia. The 1-year mortality was higher in patients with myocardial infarction but not in patients with subclinical myocardial ischemia.[35] Nevertheless, because patients were included between 1988 and 2002, CK-MB was used and this biomarker has been clearly outdated by troponin. Our results emphasize the fact that a rise in troponin levels should carefully be interpreted according to ECG modifications in elderly patients with hip fracture.

Several points should be discussed to explain the discrepancy between our results and those of previous studies. First, in these studies,[6,34] only short-term outcome was assessed, whereas we assessed long-term (i.e., 6 months) outcome. Following hip fracture, in-hospital mortality ranges from 2.3% to 13.9%, but the risk persists beyond the immediate surgical period with 6-month mortality rates ranging from 12% to 23%. Subsequently, the mortality risk returns to that of an equivalent elderly population without hip fracture.[24] Thus, our study was probably underpowered to detect a change in in-hospital mortality but was appropriate to detect a difference in long-term outcome, which is more clinically relevant in the elderly patients.[22] Second, the proportion of elderly patients in the VISION study was low (24%) and the prognosis associated with ITR may be different in young and elderly patients, mainly because the clinical significance of this elevation might be different. Third, our elderly population had much many comorbidities (Table 1), which are known to markedly interfere with postoperative complication and outcome. Emergency conditions were also constant in our population, whereas they occurred only in a low proportion (14% in the VISION study, 21% in the Van Weas et al's study) of patients, and these emergency conditions are also known to interfere with postoperative complication and outcome. It should be noted that 30-day mortality was 1.8% to 3% in previous studies[6,34] versus 8.0% in our study. This greater exposure to high-risk conditions may have overcome the hypothetical risk associated with ITR. Fourth, in a geriatric population, an ITR may be more frequently because of nonischemic events, such as pulmonary embolism, atrial fibrillation, or congestive heart failure. Importantly, we have observed a lower clearance of creatinine in the ITR group. This association has previously been reported and is not necessarily associated with a cardiac ischemic event,[36–38] particularly when considering cTnI. Again, the incidence of renal failure is markedly increased in comorbid elderly patients, particularly during emergency conditions. Lastly, we performed a strict interpretation of ECG modifications using an expert panel blinded for troponin values, offering a precise diagnosis of ACS, which was not possible in the other studies.[6] This point is important since ECG analysis may be more difficult in elderly patients who frequently present with age and/or comorbidities-related ECG modifications.

Our study has several strengths. We prospectively collected detailed assessment of comorbidities and ECG modifications, to allow troponin rise interpretation. The definition of ACS group responded strictly at the universal definition of myocardial infarction and all ECGs were independently interpreted by an expert panel blinded to troponin values. The procedures used in our UPOG were used for all patients, and we have previously demonstrated a significant reduction of 6-month mortality and rehospitalization.[24]

Our study has several limitations. First, this study must be considered as essentially retrospective. Nevertheless, data were collected prospectively and the statistical plan was determined before the analysis. Second, the sample size in the ITR group was relatively low (n = 50) and thus the power of our study may have been insufficient to show a significant difference. Nevertheless, it should be pointed that the difference observed between the ITR and Control groups was very low (Fig. 2), suggesting that, even if it exists, this difference is probably not clinically significant. Moreover, looking at many other outcome variables, we failed to identify any poor prognosis signal in the ITR group. Third, we did not use the ultrasensitive method of analysis of troponin. However, we do not think that this point may have interfered with our results as ultrasensitive method may have only detected even more subtle increase in troponin without clinical significance. Fourth, we did not systematically measure preoperative cTnI and we cannot rule out the possibility that some patients had chronically elevated cTnI concentrations that were unchanged postoperatively, particularly those with chronic renal failure. Fifth, we did not measure preoperative cTnI in all patients but, in previous studies, preoperative troponin measurements before elective surgery was not significantly associated with poor outcome.[39] Lastly, our results may not apply to other orthogeriatric models reported in the literature.[16–21] Our model is essentially characterized by an early admission to a dedicated geriatric unit, a high rate of early surgery (i.e., <24 hours after admission),[22] and this model has been shown to markedly decrease mortality and improve autonomy, walking ability, and functional status.[24]

In conclusion, in elderly patients with hip fracture, ITR is not associated with a significant increase in death and/or rehospitalization within 6 months or any other outcome variable. In this elderly and comorbid population, troponin rise should be strictly interpreted with consideration for universal definition of myocardial infarction, requiring a detailed analysis of ECG modifications.

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