

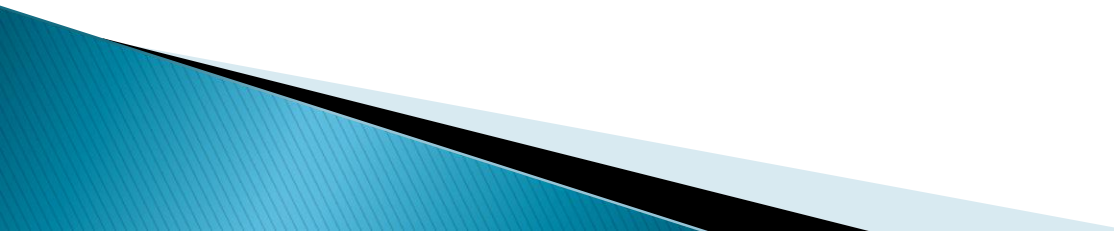
➤ Comparison of Outcomes in Patients with Acute Coronary Syndrome Presenting with Typical vs Atypical Symptoms

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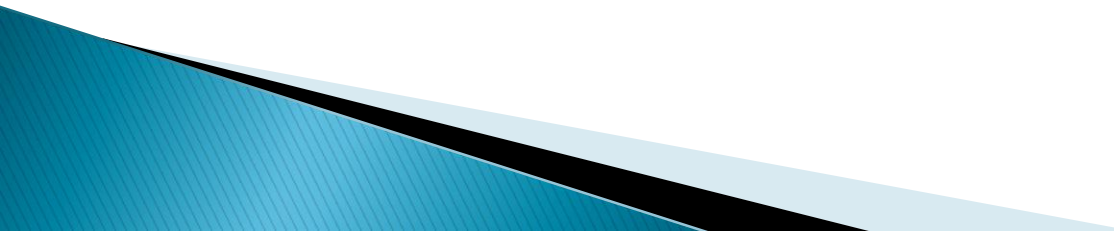
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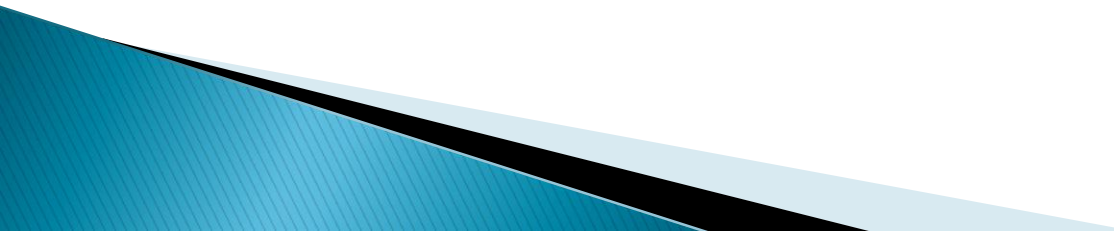
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Abstract

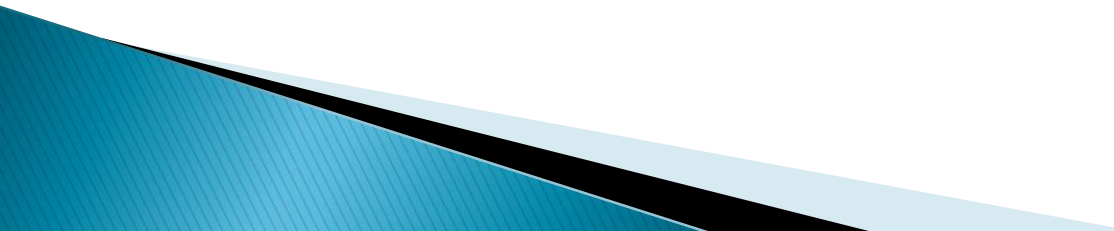
- Although typical chest pain is an important clinical feature required for diagnosis of Acute Coronary Syndrome (ACS), many patients present with atypical complaints.
 - The full extent and implication of this presentation is largely unknown. The study aim was to evaluate possible relationships and temporal trends between presenting symptoms and outcomes in patients with ACS.
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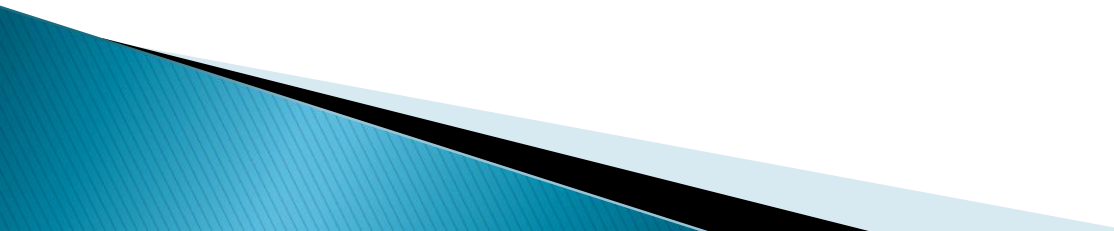
- ACS patients who present with atypical complaints have a less favorable outcome compared with patients who present with typical chest pain, and failed to show an improvement in mortality over the past two decades.
 - Identification and utilization of guideline recommended therapies in these high-risk patients may improve their future outcome.
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➤ Introduction

- Typical chest pain is considered a cardinal clinical feature required for ACS diagnosis. However, some patients present with atypical complaints, which may result in delayed diagnosis, both due to late hospital arrival and under diagnoses by the primary caregiver. This population of patients with atypical complaints is not well characterized, although some studies suggest a higher incidence in women and older patients and in patients with peripheral arterial disease or cancer.
- The data on relations between presenting symptoms and ACS outcomes are scarce and contradictory.
- They sought to investigate whether the presenting symptoms of ACS patients are associated with their outcomes, and to examine temporal trends in the management and outcomes of these patients in the last 2 decades.

Methods

- The ACS Israel Survey (ACSIS) is a biennial prospective national registry of all patients with ACS who are hospitalized in 25 coronary care units and cardiology departments in all general hospitals in Israel, over a 2-month period (March to April). Clinical, historical, and demographic data were recorded on pre-specified forms for all admitted patients diagnosed with ACS. Patients for whom the diagnosis of ACS was uncertain were omitted from the registry.
 - Included in the present study were all patients enrolled in the ACSIS registry during 2000–2016,
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- ▶ Patients were divided into two main groups :
 - ▶ the first group included patients who presented with typical chest pain (for whom typical chest pain was marked as their primary complaint)
 - ▶ and the second group included patients who presented with a primary complaint other than typical chest pain, for whom one of the following complaints was marked – nonspecific chest pain, dyspnea, palpitations and other.
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- ▶ In order to create a more homogenous population, they excluded patients admitted with an initial complaint of syncope or sudden cardiac death – for whom prognosis is known to be much worse. Patients who presented with typical chest pain and an additional complaint (e.g. dyspnea or palpitations) were classified as having a typical chest pain.
 - ▶ Clinical outcomes included 30 days major adverse cardiac events (30d MACE) which included death, myocardial infarction (MI), stroke, unstable angina, stent thrombosis, urgent revascularization, 30 day all-cause mortality and 1-year all-cause mortality.
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Results

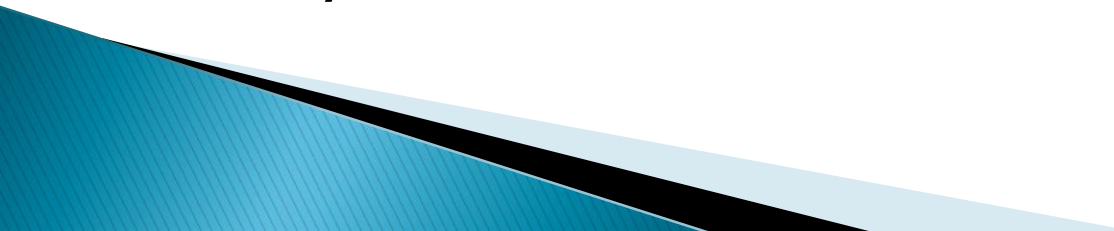
- ▶ During 2000–2016, 14,722 ACS patients were enrolled in the ACSIS registry. Of them, 11,508 (78%) presented with typical chest pain, and 3214 (21%) with an atypical complaint. ➡
- ▶ Compared with patients with typical chest pain, those who presented with **atypical complaints** were more likely to be **older**, **female**, and **with more comorbidities** such as hypertension, diabetes mellitus, renal dysfunction and heart failure; but less likely to have dyslipidemia or be an active smoker. ➡
- ▶ Patients with **atypical complaints** were more likely to present with **a NSTEMI**, compared with patients who presented with typical chest pain and had a significant delay in primary assessment, which was expressed as longer time to first ECG and longer duration from onset of pain to an examination by a primary caregiver (Table 2) ➡
- ▶ Coronary angiography was performed less frequently in patients who presented with atypical complaints, compared with patients who presented with typical chest pain, which in turn resulted in lower rates of percutaneous coronary intervention for this group (Table 2). ➡

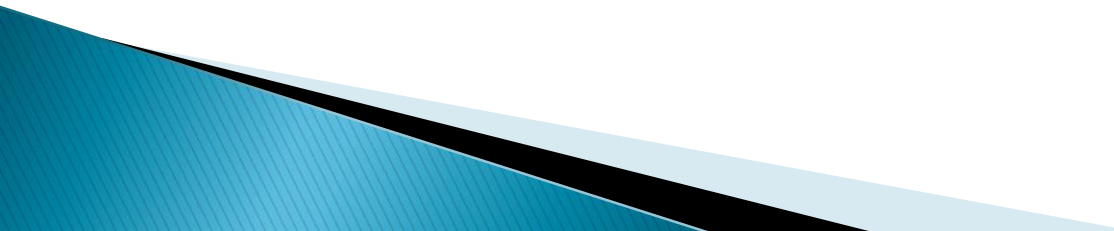
- ▶ The rate of 30-day MACE, 30-day mortality, and 1-year mortality were significantly higher in patients presenting with atypical complaints, compared with those presented with typical chest pain . This difference was evident both in patients with STEMI and in those with NSTEMI-ACS ➡
 - ▶ A temporal trends analysis comparing the period of 2000–2006 to that of 2008–2016, demonstrated a significant improvement in 1-year mortality in the late period for patients who presented with typical chest pain (6.2% vs. 9%, $p < 0.001$), while patients who presented with atypical complaints showed no improvement in 1-year mortality over time (15.6% in both early and late period) . ➡
 - This difference was evident both in STEMI and NSTEMI-ACS patients, but more pronounced in STEMI patients.
 - While 30 day MACE decreased significantly over the past two decades in both groups, the improvement was more pronounced in patients with typical chest pain (18.2% vs. 9.2%) than in those with atypical complaints (19.2% vs. 14.9%).
- Among patients with atypical complaints, NSTEMI-ACS patients did not show any improvement over time .

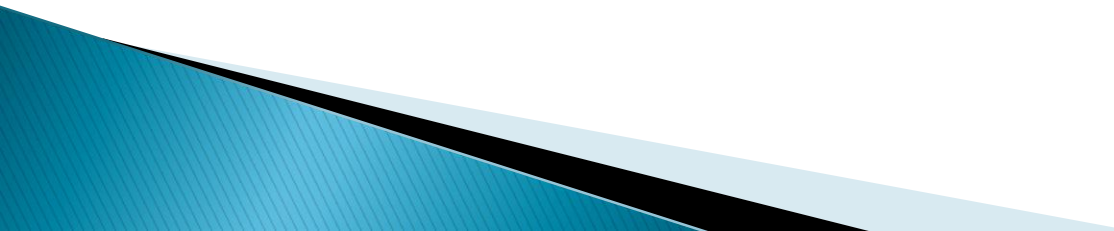
- ▶ Propensity score analysis was performed that included the following variables: age, gender, current smoking, hypertension, dyslipidemia, diabetes mellitus, family history of CAD, prior MI, prior CABG, prior CVA/TIA, prior CHF, Killip class and prior chronic kidney disease.
- ▶ After the matching procedure, 7623 and 2421 patients with typical chest pain and atypical complaints remained, respectively.
- ▶ One year mortality was still significantly higher in patients who presented with atypical complaints (11.8% vs. 9.2%, $p < 0.001$), (Fig. 4), and this difference was evident mainly in STEMI patients (Fig. 4S).



Discussion

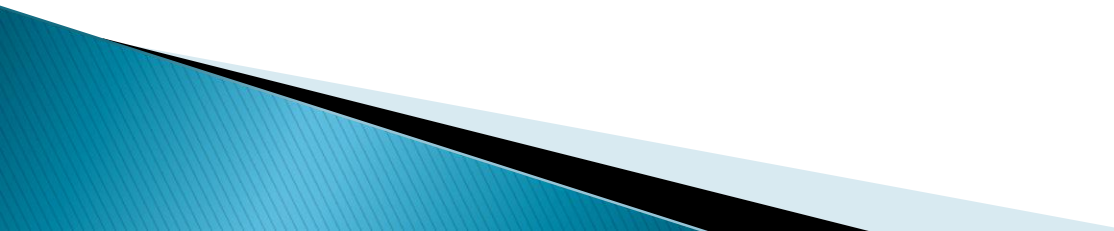
- ▶ In this study of patients with ACS in a prospective biennial national registry, it is evident that patients who presented with atypical complaints had increased rates of 1-year mortality, 30-day mortality, and 30-day MACE compared with those who presented with typical chest pain. Moreover, despite the improvement in different treatment strategies over the years, only patients who presented with typical chest pain had improved outcomes in the late (2008–2016) compared with the early period (2000–2006). Outcomes of patients who initially presented with atypical complaints did not seem to change over the years.
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- ▶ In order to provide the patient with prompt and adequate treatment, timely recognition of patients with ACS is crucial. One out of five patients in our cohort presented with atypical complaints, an incidence that emphasizes the prevalence of these patients in our day to day routine.
 - ▶ The evidence regarding the relationships between presenting symptoms and outcomes in ACS patients is scarce, and few studies have examined this issue.
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- ▶ Patients who presented with atypical complaints tended to have more comorbidity . This higher prevalence of different comorbidities might reflect a worse prognosis to begin with, but on the other hand might blunt typical anginal pain.
 - ▶ Moreover, patients with atypical complaints waited a longer time for a first ECG to be performed that probably reflects the difficulties in recognizing these patients and providing them with appropriate treatment.
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- ▶ Because STEMI and NSTEMI-ACS patients do not always share the same population characteristics (STEMI patients tend to be younger, more often male, and have fewer comorbidities), a separate analysis was performed for STEMI and NSTEMI-ACS patients. While worse outcomes were found in both STEMI and NSTEMI-ACS patients who presented with atypical complaints, STEMI patients who presented with atypical features had worse outcomes compared to NSTEMI-ACS patients .

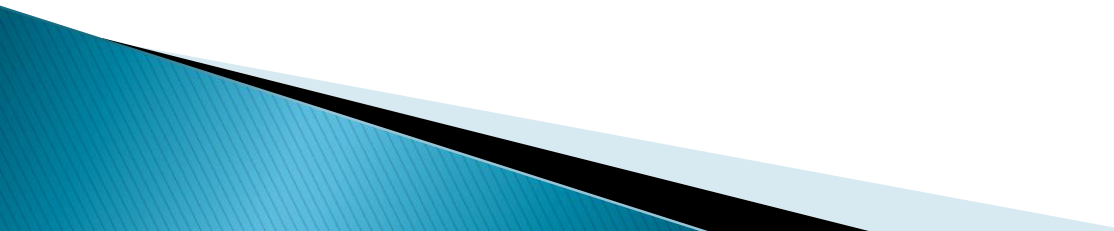


- ▶ Despite continuous efforts to improve diagnostic and treatment strategies in ACS, a temporal trends analysis revealed that for patients who presented with atypical complaints, outcomes have not significantly improved over the past two decades. This finding emphasizes that these patients might "slip under our radar" and not be treated properly. An effort should be made to timely identify these patients by careful history taking, a proper physical examination, and the use of highly sensitive biomarkers and different imaging modalities.
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limits

1. this study has several limitations.
2. Results are derived from the ACSIS registry, which is comprised of a population admitted to cardiology wards and intensive cardiac care units nationwide with the diagnosis of ACS, therefore patients who were admitted to an internal medicine ward might not be represented in this study.
3. In addition, the ACSIS registry has limited follow-up data beyond the index hospitalization with respect to long-term medical treatment, adherence to treatment, cause of death and additional interventions. Therefore, the long-term outcomes may be significantly influenced by these and other post discharge intervening factors.
4. In addition, this study is an observational study, and therefore a definite causal relationship between the natures of the initial complaint of the patient to their outcomes cannot be ascertained.
5. Last, despite existence of clear definitions of “typical” and “atypical” in the ACSIS operating manual, our data collection may be susceptible to ascertainment bias.

conclusion

- ▶ In conclusion, ACS patients who present with atypical complaints have a less favorable outcome compared with patients who present with typical chest pain. Moreover, ACS patients who presented with atypical complaints failed to show an improvement in mortality over the past two decades. Identification and utilization of guideline-recommended therapies in these high-risk patients may improve their future outcome.
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Thank you
for your attention



Figure 1 – Kaplan–Meier curves for 1-year all-cause mortality according to symptoms at presentation.

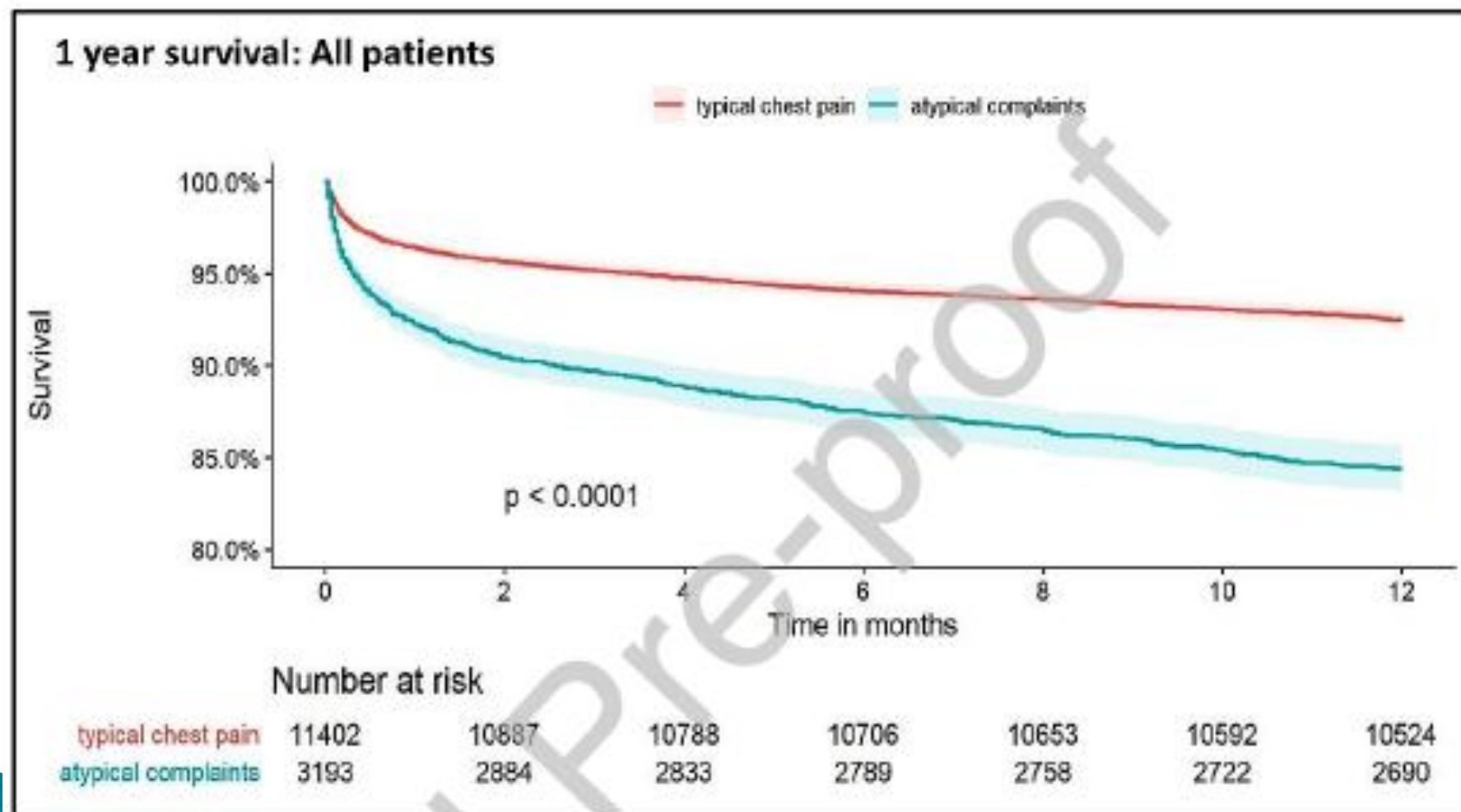


Figure 2 – Temporal trends analysis for 1-year all-cause mortality according to symptoms at presentation during the early period (2000–2006) compared with late period (2008–2016).

1 year survival: All patients

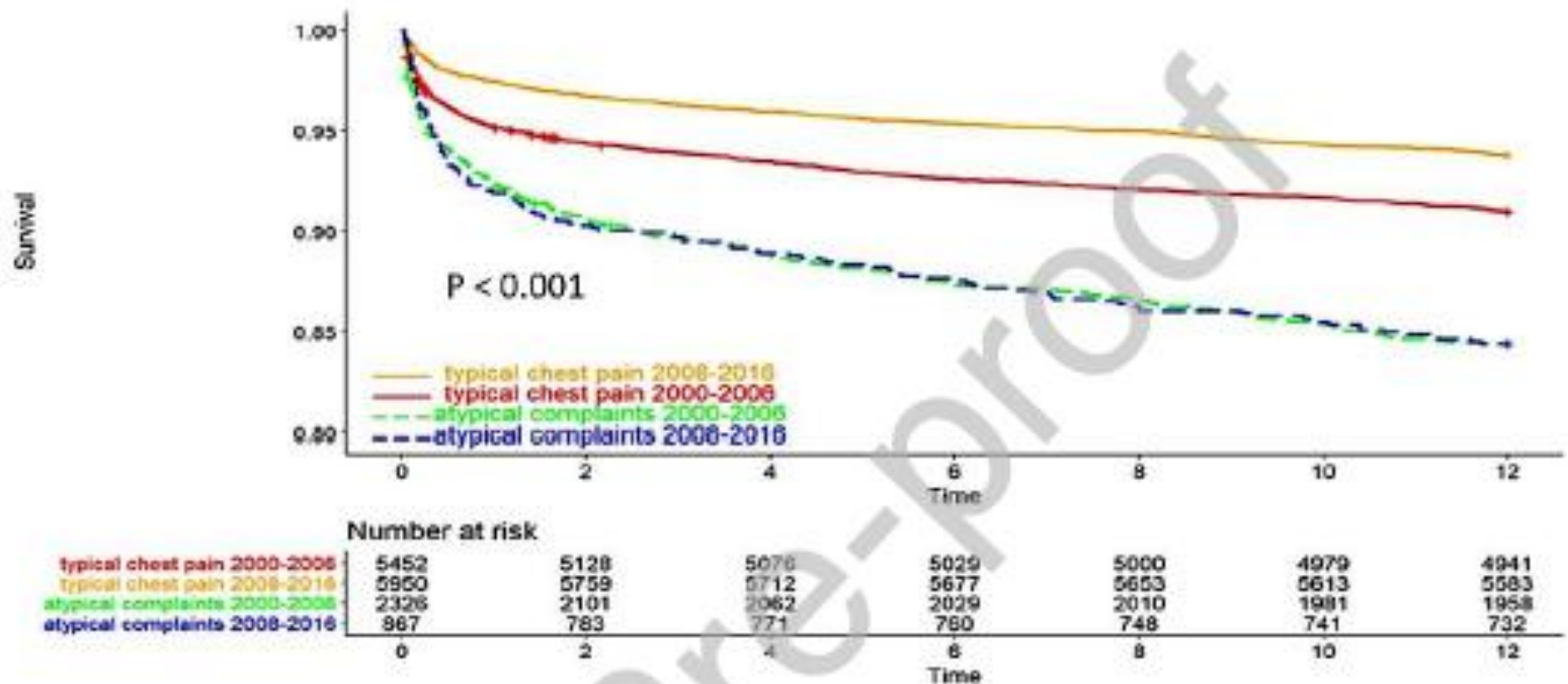


Figure 3 – Cox regression analysis and hazard ratios (HR) for 1-year all-cause mortality according to different co-variates.

COX models: HR for 1 Year Mortality with 95% CI

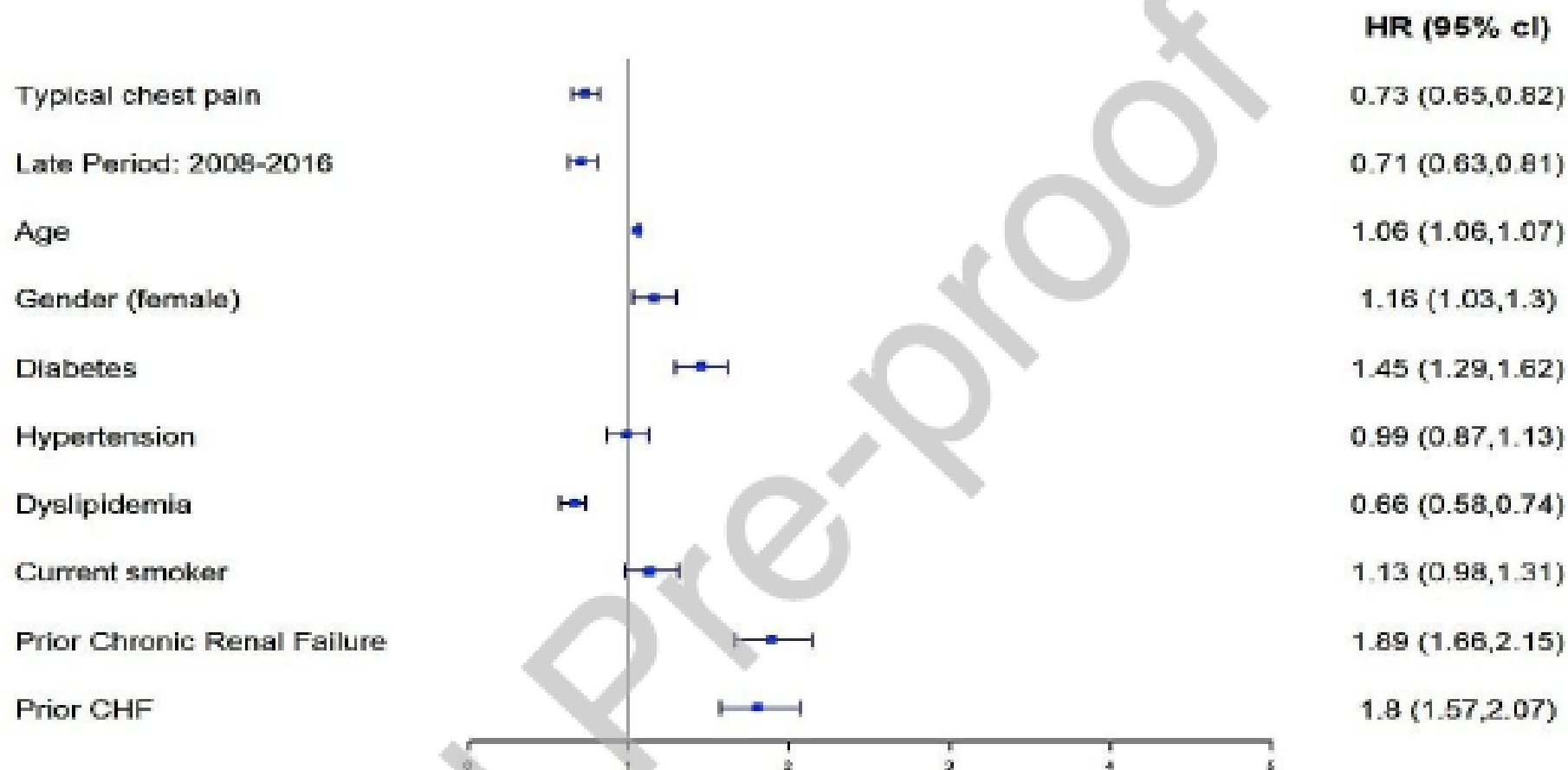


Figure 4 – Kaplan–Meier curves for 1–year all-cause mortality after propensity score matching according to symptoms at presentation.

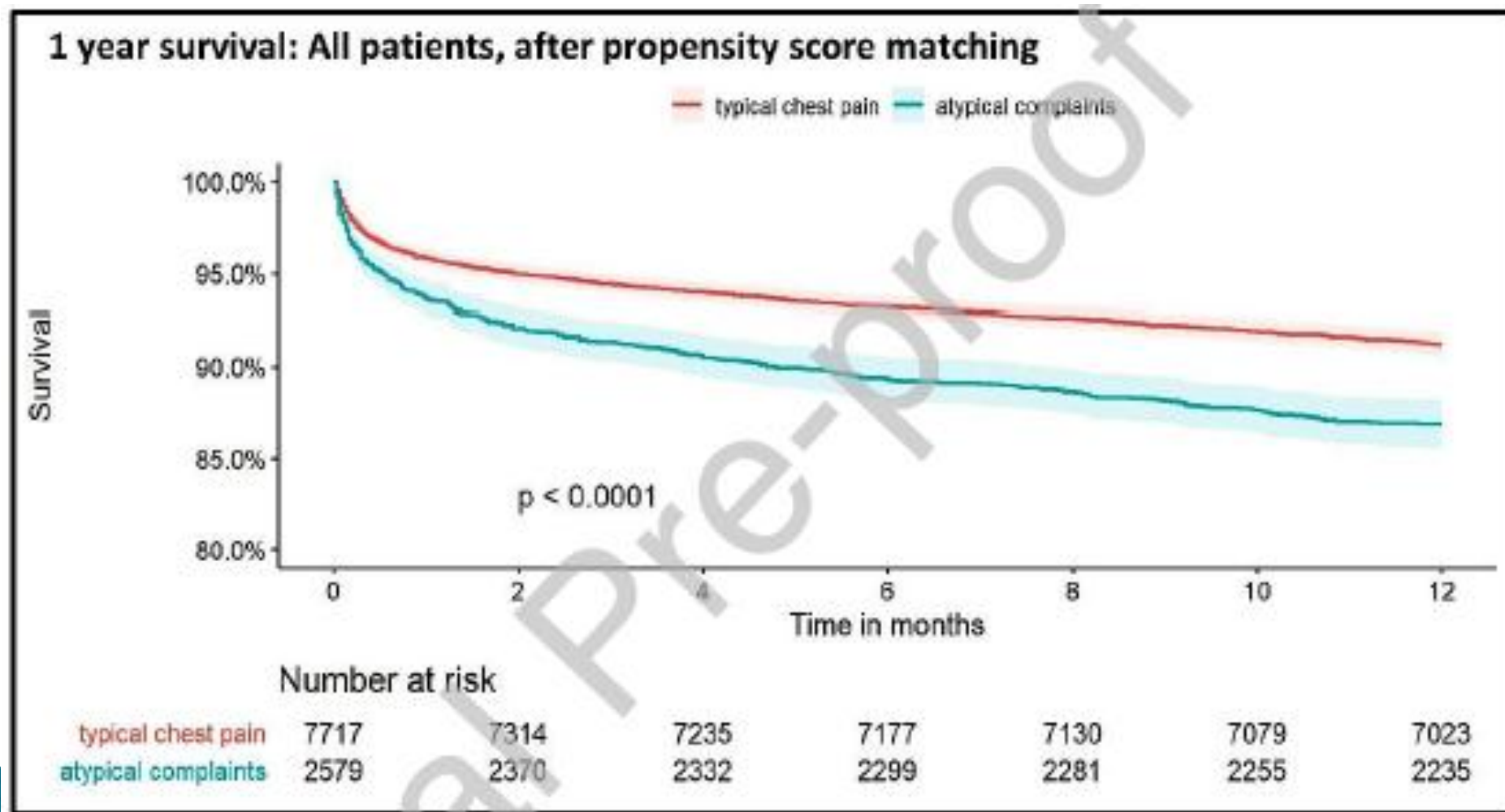


Table 1 - Baseline characteristics

Chest Pain

Variable	Typical (n = 11508)	Atypical (n = 3214)	p value
Age (years, mean±SD)	62.9±12.7	66.8±13.3	<0.001
Women	2454 (21.3%)	931 (29.0%)	<0.001
Dyslipidemia*	7597 (66.3%)	1903 (59.6%)	<0.001
Hypertension	6567 (57.3%)	2050 (64.1%)	<0.001
Current smoker	4488 (39.3%)	909 (28.6%)	<0.001
Diabetes mellitus	3947 (34.4%)	1276 (39.9%)	<0.001
Family history of coronary artery disease	2844 (26.4%)	634 (21.1%)	<0.001
Body mass index (kg/m ²), mean±SD	28.1±11.5	27.7±9.1	0.1
Prior myocardial infarction	3492 (30.4%)	1010 (31.5%)	0.2
Prior coronary artery bypass graft	1096 (9.6%)	387 (12.1%)	<0.001
Chronic kidney disease**	1094 (9.5%)	491 (15.4%)	<0.001
s/p Cerebrovascular event/Transient ischemic attack	825 (7.2%)	345 (10.8%)	<0.001
Estimated glomerular filtration rate (ml/min), median [Q1,Q3]	76 [60, 92]	68 [48, 85]	<0.001
Heart failure	720 (6.3)	426 (13.3)	<0.001

58.6 % non-specific chest pain

28.1% dyspnea

4.7% palpitations

23.3 % complaint classified as "other".

Values are presented as n (%) unless otherwise specified.

* Dyslipidemia was defined if the patient had a previous history of dyslipidemia, according to his personal medical file.

**CKD was defined as creatinine ≥ 1.5 mg/dL, creatinine clearance < 50 ml/min, or on dialysis.

Table 2 - Characteristics of index ACS

Variable	Presenting complaint		p value
	Typical (n=11508)	Atypical (n=3214)	
STEMI on presentation	5595 (48%)	1100 (34%)	<0.001
Time from symptoms onset to first medical contact (minutes)	110 [40, 360]	120 [44, 443]	0.01
Time from first medical contact to first electrocardiogram (minutes)	21 [7, 62]	51 [18, 100]	<0.001
Time from pain onset to urgent primary percutaneous coronary intervention (minutes)	329±554	487±668	<0.001
Coronary angiography during hospitalization	9550 (83.0%)	2277 (70.8%)	<0.001
Percutaneous coronary intervention during hospitalization	7368 (64.0%)	1563 (48.6%)	<0.001
Coronary artery bypass graft during hospitalization	557 (4.9%)	143 (4.5%)	0.4
Normal sinus rhythm on electrocardiogram	9039 (90.0%)	2477 (84.5%)	<0.001
Killip class III/IV on admission	431 (3.8%)	482 (14.9%)	<0.001

Values are presented as n (%), mean ± SD or median [Q1, Q3].
STEMI: ST elevation myocardial infarction

Table 3 - Clinical outcomes

Presenting complaint			
Variable	Typical	Atypical	p value
Entire cohort			
30 day rehospitalization	2017 (17.5%)	566 (17.6%)	0.6
30 day MACE	1549 (13.5%)	580 (18.0%)	<0.001
30 day Mortality ^a	409 (3.6%)	246 (7.7%)	<0.001
1-year mortality ^{a, b}	857 (7.5%)	497 (15.5%)	<0.001
STEMI patients			
N	5595	1100	
30 day rehospitalization	985 (17.6%)	181 (16.5%)	0.8
30 day MACE	815 (14.6%)	232 (21.1%)	<0.001
30 day Mortality ^a	274 (4.9%)	129 (11.8%)	<0.001
1-year mortality ^{a, b}	455 (8.2%)	202 (18.5%)	<0.001
NSTEMI-ACS patients			
N	5906	2112	
30 day rehospitalization	1032 (17.4%)	385 (18.2%)	0.4
30 day MACE	733 (12.4%)	348 (16.5%)	<0.001
30 day Mortality ^a	135 (2.3%)	117 (5.6%)	<0.001
1-year mortality ^{a, b}	400 (6.8%)	294 (14.0%)	<0.001

Values are presented as n (%). Minor discrepancies are due to missing data.

^a 30 day and 1 mortality refer to all-cause mortality.

^b Percentages are Kaplan- Meier rates.

