Measuring quality of care in the treatment of acute coronary syndrome

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Chapter 3

The occurrence and preventability of adverse events in patients with acute coronary syndrome.

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ABSTRACT:

AIM: Adverse events as a result of hospital care occur frequently. However, data on adverse events in acute care settings are scarce. Hence, our aim is to gain insight in the occurrence and preventability of adverse events and to identify patients at increased risk for an adverse event in acute cardiac care.

METHODS & RESULTS: Patients (n= 879, 64 ± 12 years, 71% male) presenting with an acute coronary syndrome in a tertiary care center warranting coronary angiography in 2012 and 2013 were included. Trained physicians performed a structured patient record review to screen for the nature, occurrence and preventability of adverse events during admission. During 2,999 days of admission, 143 adverse events occurred in 116 patients (13%), of which 35 (3%) were considered to be preventable. Older age, female sex and decreased renal function were predictors of adverse events in patients with a coronary syndrome.

CONCLUSION: Harm due to health care is a serious problem in ACS patients. Research on patient safety on a departmental level is important, and safety should be considered a core value in a care organization.

INTRODUCTION

The primary goal of medical care is to discharge the patient in the best possible health condition, thereby avoiding harm and subsequent hospitalizations. Unfortunately, medical care sometimes results in (potentially preventable) medical errors, disability or death, emphasizing that patient safety can still be improved.[1] Since the publication of the *To Err is Human* report in 1999 by the National Academy of Medicine, an increased sense of urgency to improve patient safety resulted in increasing numbers of hospital safety programs.[2] Motivated by success stories of non-medical industries, such as aviation and chemical industries, the first retrospective patient record review study was conducted as part of the Harvard Medical Practise Study, after which many studies in different countries followed that conducted patient record reviewing on a national level. These studies reported harm due to healthcare (e.g. adverse event (AE)) rates of 2.9 % to 16.6% based on all admissions. In addition, these studies found a significant number of patients experiencing death or permanent disability due to healthcare management errors, rather than due to the underlying disease process.[1, 3-11] Notably, a significant part of these AEs were deemed preventable (20-70%).

Currently, the focus seems to be shifting from patient record review on a hospital or national level to record reviewing on a departmental or disease-specific level as this might provide more insight into specific potential improvement opportunities. Especially strictly defined care programs, like the care for acute coronary syndrome (ACS) patients, seem to be suitable for record review. These programs have structured and clearly defined steps of procedures and interventions, which are in some way comparable to applying Lean Six Sigma in other industries. Hence, deviations from this care program might suggest potential care problems or a lack of efficiency and can therefore provide a unique starting point to examine opportunities to optimize the care program and improve patient safety [12]. We recently published a study describing the development of a validated method for patient record reviewing, based on identifying deviations in the care process of a strictly defined care program, in a patient population with ACS.[13] Hence, this method offers an opportunity to gain insight in the occurrence and preventability of AEs and to identify patients at increased risk for an AE.

METHODS

Patient population

Since 2004, all patients admitted to Leiden University Medical Center on suspicion of an ACS warranting coronary angiography, are evaluated and treated according to a strict

protocol (the MISSION! Protocol), based on evolving guidelines as was previously described in detail.[14-16] For the current study, patients treated in 2012 and 2013 for unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI) were selected, based on the discharge diagnosis.

STEMI was defined in the presence of symptoms of angina lasting longer than 30 minutes with typical electrocardiographic changes (ST-segment elevation ≥ 0.2 mV in ≥ 2 contiguous leads in V1 through V3, or ≥ 0.1 mV in other leads, or presumed new left bundle branch block.[17] An NSTEMI patient showed elevated biomarkers, but showed no ST-elevation during admission. Patients without elevated biomarkers were diagnosed as unstable angina.

The current study focussed on the in-hospital program (early reperfusion, diagnostic trajectory like echocardiography, structured medical therapy, and disease education). At the time of inclusion the preferred approach for angiography in this study population was femoral access. Patients treated with coronary artery bypass grafting were excluded for the current analysis, since the standard protocol could not be followed. The study protocol was approved by the Medical Ethics Committee of the Leiden University Medical Center, The Netherlands. The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Evaluation for adverse events

A structured medical record review, based on the method of the Harvard Medical Practice Study, to assess the occurrence and preventability of AEs was performed by two trained independent physician reviewers.[10] A comprehensive description of the method and the prior screening of process deviations and its inter-rater reliability was reported previously.[18] In brief, the first phase involved a medical record review of process deviations. A process deviation was defined as every procedure or treatment that differed from the MISSION!-protocol, such as additional procedures (a pacemaker implantation or second percutaneous coronary intervention), prescription of extra medication other than described in the protocol (use of anti-arrhythmic drugs, anti-coagulation, inotropics or diuretics) or omission of a procedure (no diagnostics performed). If a process deviation was present, the patient record entered a second phase in which an assessment was performed on whether the event resulted in harm to the patient. Patient harm or any disadvantage for the patient that resulted in prolonged or strengthened treatment, temporary or permanent (physical and/or mental) impairment or death and caused by medical care was defined as an AE. If so, it was rated whether it was preventable (and therefore caused by an error). The causation score of an AE, as well as the preventability score, were scored on a 6-point-Likert scale and noted as caused by health care or preventable if the score was 4 to 6. When more than one AE occurred in a patient, both were registered. The inter-rater reliability was

assessed for 10% of the patients (n=87) by an independent cardiologist, who was blinded to the outcome of the first review. On a patient level, there was an agreement in 73 patient records (agreement level of 84%). The κ statistics of the causality was substantial (κ 0.67 (95% CI 0.51 to 0.83).[13]

Classification of an adverse event

AEs were classified by severity (leading to possible injury, temporary injury, permanent injury or death), nature (e.g. as a consequence of taken medication, procedural activities, diagnostic activities or other clinical activities) and causal factors (technical, human, organizational or patient-related factors) were noted.[19] In case the assessment of the physician reviewer(s) was inconclusive, an expert panel, consisting of four experienced cardiologists, was consulted in order to come to an agreement regarding the causality or preventability. Examples of the classification of preventable adverse events are shown in **Table 1**.

Clinical characteristics

Clinical characteristics were added to the protocol to correlate clinical parameters with AEs. Infarct characteristics were collected, such as diagnosis, percutaneous treatment, peak troponin-T and creatine kinase. Furthermore, comorbidities such as hypertension (defined as blood pressure ≥140/90 mmHg or previous pharmacological treatment), hyperlipidaemia (defined as total cholesterol ≥190 mg/dl or previous pharmacological treatment), a diagnose of diabetes mellitus (insulin and non-insulin-dependent), history of pulmonary diseases and renal clearance (calculated with the Chronic Kidney Disease Epidemiology Collaboration equation, presented in 10 mL/min/1.73m^2) at admission were noted.[20]

Statistical analysis

Continuous variables are presented as means with standard deviations or medians with 25th and 75th percentiles where appropriate. Dichotomous variables are presented as numbers and percentages.

AE rates were reported by the proportion of patients with at least one AE and the number of AEs per 1,000 patient days. In the calculation of the 95% confidence interval (95%-CI) for event rates, a Poisson distribution of the observed number of events was presumed. To obtain a risk estimation of experiencing an AE, demographic variables and comorbidities known at baseline were used to conduct a logistic regression. First, the baseline variables are studied in a univariate logistic regression model, with experiencing an AE as binary outcome. For each variable an odds ratio with a p-value and 95%-CI was calculated. Variables with a p-value ≤ 0.10 are further evaluated in a multivariate logistic model, using backward stepwise selection. At each step, the least significant variable was discarded from the model, until all variables in the model reached a p-value ≤ 0.05.

Table 1: Examples of the determination of an preventable adverse event.

Nature	Example of a preventable adverse event
Diagnostic activities	*Despite evolving electrocardiographic changes during the weekends, percutaneous coronary intervention was delayed.*
	Human factors as causal factor of the event.
Drug-related adverse event	*Hypotensive episode after a double dose of antihypertensive therapy due to miscommunication between patient and nurse.*
	Organizational factor as causal factor of the event.
Other clinical activities	*Traumatic placement of urinary bladder catheter in patients with triple antiplatelet therapy, resulting in bladder lavage.*
	Human factors as causal factor of the event.
Other non-procedural activities	*None of the preventable adverse events was related to non-procedural activities.*
	N/A
Procedural activities	*Substantial renal dysfunction due to contrast given by the coronary angiography in a patient known with acute on chronic renal disease,, in which delayed consultation of the internal medicine department.*
	Patient-related factor as causal factor of the event.
Causal factors	
Human factors	*Late detection of subcutaneous edema due to intravenous infusion.*
	Other clinical activities as nature of the event.
Patient-related factors	*Delirium post infarction in high-aged patient and immobile by intra-aortic balloon pump without actively taken preventive measures.*
	Other clinical activities as nature of the event.
Technical factors	*None of the preventable adverse events was related to non-procedural activities.*
	N/A
Organizational factors	*Late detection of massive groin hematoma leading to death.*
	Procedural-related as nature of the event.
Not judgeable	*Staphylococcus aureus bacteraemia due to phlebitis of a peripheral intravenous drip of unknown duration.*
	Other clinical activities as nature of the event.

RESULTS

Population

In 2012 and 2013, 879 patients were evaluated and treated for an ACS. As is demonstrated in **Table 2**, patients had a mean age of 64±12 years, the majority was male (71%) and 594 (68%) patients experienced a STEMI. During a median stay of three days (25^{th}–75^{th} percentile: 2 – 4), all patients underwent coronary angiography and 747 (85%) patients were treated by percutaneous coronary intervention.

Adverse events

During 2,999 days of admission, 143 AEs occurred in 116 (13%) patients in which harm was related to care received, rather than to underlying conditions. This resulted in 48 AEs per 1,000 patient days (**Table 3**). **Table 4** illustrates the characteristics of the AEs. The majority resulted in temporary injury (80%), such as a urine tract infection after urinary bladder catheter placement or temporary hypotension after administration of a double dosage of blood pressure medication. However, eight (6%) events were associated with permanent injury, and three (2%) events were associated with serious harm which likely resulted in *death* of the *patient*. Most events were the result of procedural activities (58%) and were related to human factors (55%). Patients with an AE had longer hospital stays compared to patients without an AE (median 4 days (25^{th}–75^{th} percentile: 3 – 6) versus median 3 days (25^{th}–75^{th} percentile: 2 – 4), p≤0.001). A sub-analysis showed that the patients with one or more missing variables (n = 161, 18%) were more often discharged

Table 2: Patient characteristics

	All patients	With an adverse event	Without an adverse event	p-value
	879 patients	*116 patients*	*763 patients*	
Age (years)	64 ± 12	69 ± 12	63 ± 12	< 0.001
Female sex	253 (29%)	53 (46%)	200 (26%)	< 0.001
BMI (kg/m2)	27 ± 4	27 ± 4	27 ± 4	0.976
Infarct characteristics				
Diagnosis				
STEMI	594 (68%)	77 (66%)	517 (68%)	0.425
NSTEMI	135 (15%)	22 (19%)	113 (15%)	
Unstable angina pectoris	150 (17%)	17 (15%)	133 (17%)	
Treated with PCI	747 (85%)	104 (90%)	643 (84%)	0.162
Troponine-T peak (µg/L) (median, IQR)	1.8 (0.3 – 4.8)	2.3 (0.3 – 5.2)	1.7 (0.3 – 4.7)	0.003
CK peak (U/L) (median, IQR)	705(206 – 1665)	910(243 – 1908)	687(200 – 1626)	0.188
Comorbidity				
Hypertension	352 (40%)	60 (52%)	305 (40%)	0.014
Hyperlipidemia	198 (23%)	27 (23%)	175 (23%)	1.000
Diabetes mellitus	115 (13%)	21 (18%)	99 (13%)	0.182
Known coronary artery disease	145 (16%)	23 (20%)	122 (16%)	0.347
Known pulmonary disease	88 (10%)	21 (18%)	68 (9%)	0.004
Renal clearance at admission (10 ml/min per 1.73m2)	75 ± 23	72 ± 26	75 ± 23	< 0.001

BMI = body-mass index; IQR = interquartile rang; STEMI = ST-elevated myocardial infarction; NSTEMI = non-ST-elevated myocardial infarction; PCI = percutaneous coronary intervention. Missing variables were present in: Troponin-T-peak (14%) and Creatine-Kinase-peak (14), hypertension (3%), hyperlipidemia (3%), diabetes mellitus (2%) and renal clearance (5%).

to another hospital for recovery compared to the patients with no missing variables. No differences were observed on patient characteristics (age, gender, BMI, comorbidities), infarct characteristics (diagnosis, admission duration) or the number of adverse events between the patients with one or more missing variable compared to the patient without missing variable.

Preventable adverse events

A total of 35 (3% of all patients) AEs in 34 patients were judged preventable. This resulted in 12 preventable AEs per 1,000 patient days. Three patients with permanent injury and two patient-deaths were included in this group of patients. The majority was due to procedural activities in the catheterization laboratory (49%) or other clinical activities (29%), and were caused by human factors (63%) (**Table 3&4**). Of note, 10 out of 17 AEs classified as procedural activities were related to the arterial puncture, in which a bleeding or the severity of a bleeding probably could be prevented by optimizing the chain of care and more alert observation after the procedure, or changing the arterial puncture site of the interventional procedure of high risk patients.

Table 3: Occurrence and preventability of adverse events.

	879 patients	
Days of observation, total	2,999	
Days of observation / per patient	3.4	
Length of stay (days) (median, IQR)	3 (2-4)	
Number of adverse events	143	
Number of preventable adverse events	35	
Event risk		
Number of patients with at least one adverse event	116 (13%)	(95%-CI: 11%-16%)
Number of patients with at least one preventable adverse event	34 (4%)	(95%-CI: 3%-5%)
Event rate		
Adverse event rate	48 per 1,000 patient days	
Preventable adverse event rate	12 per 1,000 patient days	

Risk estimation

To determine specific parameters correlated to an increased risk for an AE, the univariate regression model shows that age>70 years (OR 2.5 (95%-CI 1.7 – 3.6)), female gender (OR 2.4 (95%-CI 1.6 –3.5), hypertension (OR 1.6 (95%-CI 1.1 – 2.4)), pulmonary disease (OR 2.3 (95%-CI 1.3 – 3.9), and renal clearance (OR 0.9 (95%-CI 0.9 – 1.0) were predictors of AEs (**Table 5**). The type of infarction (STEMI/NSTEMI) was not significantly associated with the risk for an AE. Using multivariate analysis, patients > 70 years (OR 1.6 (95%-CI 1.0 – 2.6), p=0.042), female sex (OR 3.7 (95%-CI 2.2 – 6.3), p≤0.001) and poor renal function

(OR 0.8 (95%-CI 0.8 – 0.9), p=0.002) were significantly associated with an increased risk for AEs.

Table 4: Adverse event characteristics

	143 adverse events	35 preventable adverse event
Consequences of the adverse event		
Possible injury	18 (13%)	1 (3%)
Temporary injury	114 (80%)	29 (83%)
Permanent injury	8 (6%)	3 (9%)
Deceased	3 (2%)	2 (6%)
Nature		
Diagnostic activities	3 (2%)	3 (9%)
Drug-related adverse event	25 (18%)	5 (14%)
Other clinical activities	27 (19%)	10 (29%)
Other non-procedural activities	5 (3%)	0 (0%)
Procedural activities	83 (58%)	17 (49%)
Causal factors		
Human factors	78 (55%)	22 (63%)
Patient-related factors	54 (38%)	10 (29%)
Technical factors	0 (0%)	0 (0%)
Organizational factors	6 (4%)	2 (6%)
Not judgeable	5 (3%)	1 (3%)

Table 5: Correlates of patients with adverse events.

	Univariate regression OR (95%-CI)	p-value	Multivariate regression OR (95%-CI)	p-value
Age > 70 years	2.5 (1.7 – 3.6)	≤ 0.001*	1.6 (1.0 – 2.6)	0.042
Female gender	2.4 (1.6 – 3.5)	≤ 0.001*	3.7 (2.2 – 6.3)	≤ 0.001
BMI (kg/m^2)	1.0 (1.0 – 1.0)	0.976		
Comorbidity				
Hypertension	1.6 (1.1 – 2.4)	0.014*		
Hyperlipidemia	1.0 (0.6 – 1.6)	0.944		
Diabetes mellitus	1.5 (0.9 – 2.5)	0.160		
Known coronary disease	1.3 (0.8 – 2.1)	0.306		
Known pulmonary disease	2.3 (1.3 – 3.9)	0.002*		
Renal clearance (10 L/min per 1.73m^2)	0.9 (0.9 – 1.0)	0.096*	0.8 (0.8 – 0.9)	0.002

* variable was included in multivariate analysis. BMI = body-mass index; Renal clearance is calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

Additional evaluation of AE rate by age shows an increase in event rate per age-class, up to a 29% increased risk of experiencing an AE in patients older than 80 years (**Figure 1**). Furthermore, as shown in **Figure 2**, the risk for AEs was highest during the first days of admission (day 0 and 1: 73 AEs, 8% (95%-CI 6.5% – 10.4%) AE risk). A longer admission was also related to an increased risk for AEs (day 10 – 11: 2 AEs, 7% (95%-CI 0.9% – 26.8%) AE risk for the remaining patients). However, the difference is non-significant when compared to the lowest cumulative incidence (day 6 – 7, 1% (95%-CI 0.06% – 14.0%) (p=0.353) (**Figure 2**).

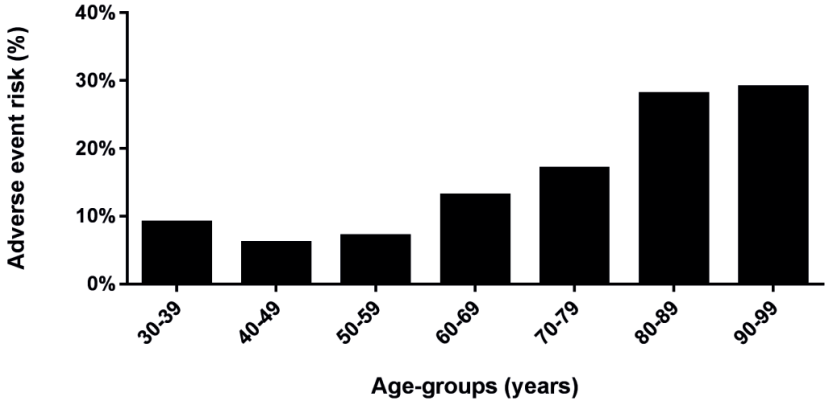

Figure 1: Adverse event risk and age.

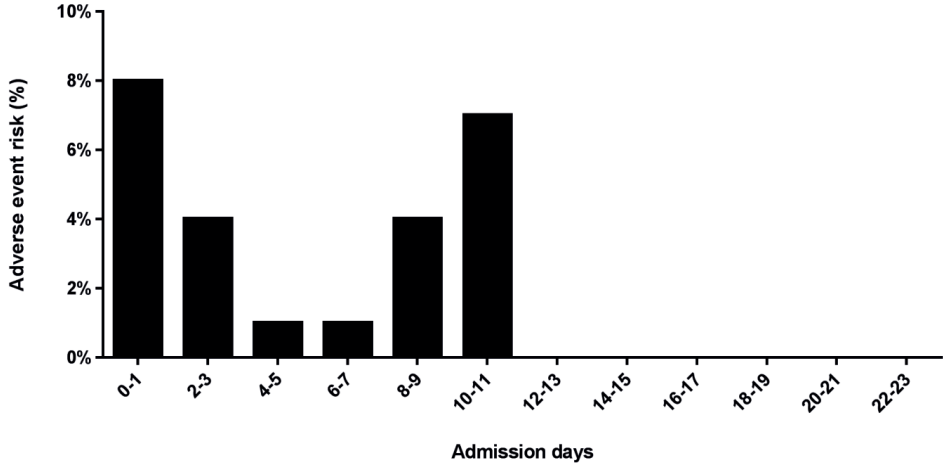

Figure 2: Adverse event risk and admission days.

DISCUSSION

In the current study on the occurrence and the preventability of AEs after treatment of an ACS, the findings can be summarized as follows: (i) 13% of the patients experienced an AE during admission and in 3% of these patients the AEs were preventable; (ii) older age, female sex and poor renal function were associated with an increased risk for AEs; (iii) incidence of AEs was highest during the first days of admission.

Occurrence

After the "*To Err is Human*" publication, an increased awareness to improve patient safety has led to an increasing number of hospital safety programs.[21] This thesis focused mainly on the (occurrence, severity, nature and causes) of adverse events, because these are more common compared to preventable adverse events and therefore more likely to be actionable on a population level. In the current study in patients treated for an ACS, an AE risk of 13% was observed. This risk is higher compared to previous national data in the Netherlands (5.7-8.0%) while being similar to worldwide registries (2.9-16.6%) which examined the risk of AEs in the general hospital population.[3-11, 22] To our knowledge, no previous record review study has been performed in ACS patients. When compared to the national data, a higher event rate in the current study could be caused by the fact that treatment of an ACS happens in an acute setting and is characterized by time-pressure decisions, patient complexity and acuity, and high risk interventions. A recent Swedish study, which also focussed on a specific population (orthopaedic patients), detected a higher AE rate (15%) compared to other local and nationwide Swedish studies.[23] Furthermore, risk factors for AEs in ACS patients have not been identified in prior studies. The current study reveals different factors influencing the risk for AEs: significantly more AEs occurred in patients with an older age, female sex, and a poor renal function. The higher risk of AE in female patients was unexpected. Although females are more likely to present with atypical symptoms of ischemia and show higher short-term mortality after acute coronary syndromes, clinical evidence is lacking on the reason why females are more susceptible to AEs.[24-26]

Preventability

An AE was defined preventable when the performance of the practitioner or health care organization falls short of the expected level of competence. In the present study, 3% of all patients experienced a preventable adverse event, which is lower when compared to other studies (28 – 70%).[3, 22, 27] Zegers et al. reported in a sub-analysis of cardiology departments in The Netherlands an AE rate of 4.9% in 1,165 admissions in which 33% was preventable.[22] Previously, McDonald suggested that the proportion of preventable AEs, particularly preventable deaths, is overestimated because of inadequate consideration of other factors

such as severity and complexity of patient disease.[28] In this study, the method and the specified population provided the opportunity to take into account the acute setting and complexity of the patients.

The majority of patients with a preventable AE recovered without permanent disability. However, two patients died as a result of the preventable AE and these cases deserve careful consideration. As stated before by Brennan et al., death associated with medical error is not preventable if death would have occurred even in the absence of error.[10] Hayward and Hoger found that many preventable deaths occurred at the end of life or in critically ill patients in whom death was the most likely outcome either during the hospitalization or in the coming months, regardless of the care received.[29] It is difficult to judge what the expected risk of death is, or would have been in the absence of an AE. Both cases were critically ill patients whose death was considered imminent. Still, their deaths could perhaps have been prevented if physicians had paid more attention to the complaints of the patient, if they would have performed more diagnostics, or if the physicians were more restrained in performing a therapeutic intervention considering the high-risk anatomy of the patient. Although the number of preventable AEs is low, the department tries to learn from these events by discussing these cases in the monthly departmental Mortality and Morbidity Review Committee Meeting The goal hereby is to create a continuous learning cycle which may improve the patient safety for all ACS patients.

The relation between admission duration and adverse events

The highest risk for a patient to experience an AE is during the first days of the admission (8% of all admitted patients). More specifically, the majority of the AEs were related to the interventional procedure (58%), which takes place during the first days (day 0&1). This study showed that the occurrence of an AE could cause a prolonged admission, which is also reported in previous studies.[30-32] Conversely, a prolonged admission may expose in-hospital patients to the occurrence of an AE. For example, a longer admission leads to a higher exposure of peripheral infusion catheters and therefore to a higher phlebitis and AE rate [33]. Likewise, serious in-hospital falls were independently correlated with an increased length of stay up to the time of fall [34]. Apparently in these patients, during a prolonged hospital stay (at day 10-11), a second, new peak in risk for AEs is observed. However, these results are based on a small number of events and are therefore non-significant. Hence, it is difficult to attribute a causal relationship between a prolonged admission and the occurrence of AEs in patients based on this study.

Future implications

Since these results are based on a single centre, this requires caution in generalizing these findings to other centres. However, this study emphasizes that research on patient safety

on a departmental level is important, and the value of safety as a core value in an organization should be embedded in clinical care. Besides, adverse events lead to a prolongation of the hospital admission and impose a large financial burden.[31, 35, 36] Considering the fact that human factors were often the cause of (preventable) AEs, it will be of interest for future research to specify these human factors in more detail, for example diagnostic errors due to a lack of knowledge, lack of coordination at discharge or lack of communication and education of the patient.

Additionally, to ensure that medical errors are reliably reported and analyses at a departmental level, a proper safety culture is warranted. A proper safety culture entails that reporting a human error is blame-free and that attention is given to optimizing the communication and teamwork between care providers.[21] Furthermore, the ultimate goal is to improve patient safety using real-time monitoring of process-deviations and AEs or, even better, to predict which patients are at risk for AEs (like female gender or a decreased kidney function) in order to prevent harm

Limitations

Some limitations have to be addressed. This study had a retrospective patient record review design and shares the limitations of all retrospective analyses. For example, overestimation in determining the causation and preventability of an event is possible when knowing its outcome. A prospective approach can augment the assessment of contributing factors of an AE.[37, 38] However, this is laborious and costly. Although judgements about the presence of an AEs are difficult and never fully objective, retrospective patient record review studies are currently one of the best methods available to assess incidence of AEs and discover latent errors.[39] Unfortunately, it was not possible to take into account all potential risk factors (e.g. thrombocytopenia, anaemia, femoral access vs. radial access) and care aspects (e.g. time of presentation of AMI (off-hours versus regular hours), subtypes of causal factors) which could potentially explain an increased risk of having an AE. Hence, more research is warranted concerning these risk factors, for example to disentangle the relation observed between gender and a higher risk for AE.

CONCLUSION

The results of this study imply that harm due to health care is a serious problem in ACS patients. During admission for an ACS, 13% of patients experienced an AE of which 24% (3% of all patients) was preventable. Patients who are older, female or with a decreased renal function are at increased risk.

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