The frequency of acute coronary syndromes and the cost of glycoprotein IIb/IIIa inhibitor treatment

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Abstract

The objective of this survey was to estimate the proportion of episodes of acute coronary syndromes (ACS) without ST segment elevation in relation to the total number of acute chest pain presentations. We attempted to estimate costs associated with glycoprotein (GP) IIb/IIIa inhibitor treatment in patients with high-risk features.

This was a prospective survey set in a typical British district general hospital, serving a population of about 300,000. It took place over a 14-week period.

The participants were all patients presenting with chest pain of possible cardiac origin, identified by intensive surveillance of all emergency medical admissions (EMAs) in patients over 16 years of age and all adult and elderly medicine in-patients. At the time of the study, the upper limit of normal for troponin T (TnT) used in this hospital was 0.05 µg/L.

The main outcome measures were: the proportion of EMAs due to chest pain of likely cardiac origin; the number of episodes of ACS without ST elevation as a proportion of all EMAs; and the projected prescribing costs of GPIIb/IIIa inhibitor treatment for high-risk cases.

We found that 22% (CI 20.07–23.5%) of all EMAs were due to chest pain likely to be of cardiac origin. One event of ACS without ST elevation was generated for every 25.6 (CI 23.8–28.6) EMAs. Using a TnT value of ≥ 0.1 µg/L to define high risk and suitability for GPIIb/IIIa inhibitor treatment, a minimum of 66% of patients with ACS without ST elevation would be eligible for treatment. In the study hospital, this translates to an annual cost of £131,000 (equivalent to £43,600 per 100,000 catchment population) or £11.45 per all-cause hospital EMA.

In conclusion, about two thirds of patients with ACS without ST elevation have high-risk features and would potentially benefit from treatment with GPIIb/IIIa inhibitors. The costs of drug treatment are appreciable, but financial planning can be assisted by the data presented here.

Key words: acute coronary syndrome, glycoprotein IIb/IIIa inhibitors, emergency medical admissions, costs, survey, cardiac chest pain

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Introduction

Patients with acute chest pain likely to be of cardiac origin account for between 20% and 30% of all emergency medical admissions (EMAs).[1,2] The National Institute for Clinical Excellence (NICE) recommends the use of GPIIb/IIIa inhibitors in high-risk ACS patients without ST segment elevation.[3] Funding for treatments recommended by NICE has been a requirement for NHS healthcare providers since January 2002.[4] Glycoprotein IIb/IIIa (GPIIb/IIIa) inhibitor treatment in acute coronary syndromes (ACS) without ST elevation may be effective in reducing the risk of death or myocardial infarction in patients who are not routinely scheduled for early revascularisation. This benefit could be up to half of the benefit seen in patients scheduled for early revascularisation.[5]

A prospective survey was conducted in order to estimate accurately the number of patients admitted annually with ACS without ST elevation and to calculate the anticipated prescribing costs of implementing the NICE recommendations on GPIIb/IIIa inhibitor treatment. Stepping Hill Hospital (SHH) is a typical district general hospital, with 298 medical beds and a notional catchment population of 300,000. There were 11,428 EMAs annually at the time of this survey. Eighty five per cent of EMA patients are Stockport Primary Care Trust residents. This population has similar characteristics to those of the English general population and a standardised mortality ratio (SMR) due to cir-

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culatory diseases of 101 (1998–2000).[6] About 15% of EMAs come from the High Peak district of North Derbyshire, which has an SMR due to circulatory disease of 123.[6]

Patients and methods

Every patient presenting with a primary complaint of acute chest pain of possible cardiac origin and admitted to SHH between August 1st, 2000 and November 12th, 2000 was included in the survey. Cases presenting with chest pain of probable cardiac origin were identified by a research nurse with a background in coronary care through daily surveillance of all emergency medical admissions, all A&E attendees and all in-patients of the medical department. The medical notes of cases were inspected and various details, including the clinical presentation and symptoms, photocopies of serial ECGs and troponin T (TnT) values, were extracted.

Cases were categorised into relevant diagnostic groups (table 1), under the supervision of two consultant cardiologists, using the definition of ACS without ST elevation based on the criteria of the British Cardiac Society and the Royal College of Physicians Clinical Effectiveness and Evaluation Unit.[7] Patients with unstable angina (UA) and non-Q-wave myocardial infarction (NQWMI) were defined as ACS without ST elevation. Not all patients with ACS without ST elevation had abnormal TnT values, as some UA patients may have normal troponin values and only minor ECG changes (table 1). Information on in-patient urgent tertiary referrals for coronary angiograms and revascularisation procedures was also collected. Apart from patients referred to tertiary centres, all other patients were treated with conservative medical management, including heparin, aspirin and intravenous nitrates, but not including GPIIb/IIIa inhibitor treatment.

Adjustment for seasonal variation was made in the calculation of expected incident cases throughout one year. This was done by the use of seasonal variation in the number of admissions routinely coded as unstable angina (ICD code I200) and subendocardial MI (ICD code I214). Confidence intervals for estimated proportions were estimated by the use of the CIA programme.[8] Prescribing costs for GPIIb/IIIa inhibitors were estimated by different risk stratification criteria,[3,9] including two TnT cut-off values (0.05 and 0.1 µg/L) and ST depression ≥ 0.1 mV in at least two ECG leads. Prescribing costs were calculated for the recommended three-day course of therapy, assuming a cost of £450 per event.[3] (This calculation does not include other costs, such as the costs of additional laboratory tests, the use of additional monitoring equipment, and the cost of referrals for tertiary investigation and treatment.)

Table 1. Chest pain diagnostic categories according to presentation, ECG picture and maximal troponin T values

Diagnostic category	Presentation
Acute coronary syndromes	
ST elevation MI	History of cardiac/ischaemic pain Sustained ST elevation in two or more limb leads Development of Q waves TnT ≥ 0.2 µg/L
Non-Q-wave MI	History of cardiac/ischaemic pain No or non-sustained ST elevation No Q wave development ECG normal or ischaemic changes TnT ≥ 0.2 µg/L
Unstable angina	History of cardiac/ischaemic pain No or non-sustained ST elevation No Q wave development AND one OR both of the following: - New ischaemic ECG changes - TnT ≥ 0.05 but < 0.2 µg/L
Other ischaemic heart disease (IHD)	
Suspected unstable angina	History of worsening cardiac/ischaemic pain No new ECG changes TnT < 0.05 µg/L Cardiac enzymes normal (if measured)
Angina	History of cardiac/ischaemic pain <20 mins No change in angina pattern recently Pain provoked by exercise/stress and relieved by rest or oral nitrates ECG may be ischaemic but unchanged TnT < 0.05 µg/L
Refractory angina	Known diagnosis of IHD Multiple admissions with chest pain ECG normal or no new changes TnT < 0.05 µg/L
Ischaemic pain secondary to systemic illness	ECG may be ischaemic TnT normal (< 0.05 µg/L) Systemic illness/other cause
Query ischaemic pain	Atypical history of pain or reason to suspect alternative cause ECG normal or no new changes TnT normal (< 0.05 µg/L)
Non-ischaemic heart disease	
Non-ischaemic pain	Definite non-cardiac cause of chest pain diagnosed e.g. pulmonary embolism, gastric, musculoskeletal

Key: TnT = troponin T

Results

Seven hundred and twenty four or 22% (confidence intervals [CI] 20.1–23.5%) of all emergency medical admissions (n=3,332) during the study period were due to acute chest pain likely to be related to ischaemic heart disease. These admissions generated 734 separate chest pain events in 672 patients. Of all chest pain events, 88 (12%) were due to ST elevation MIs: three of these patients also had a separate subsequent event of ACS without ST elevation during the same admission (table 2). There were 107 (14.8%) admissions due to ACS without ST elevation, and seven of these patients had a separate subsequent event of ACS without ST elevation during the same admission. In total, there were 117 events of ACS without ST elevation, 107 or 91.4% (CI 85–95.3%) being 'primary' events, stemming directly from an EMA, and 10 or 8.6% occurring as 'secondary' events in patients already diagnosed with ACS. Thirteen patients with ACS without

Table 2. Number of EMAs due to acute chest pain by diagnostic category, as a proportion of all EMAs due to chest pain (95% CI)

	Study period			Projected annual estimate	
Diagnostic category	**n**	**%**	**CI (%)**	**n**	**CI**
Acute coronary syndromes					
ST elevation MI	88	12	9.8–14.5	363	293–434
ACS without ST elevation (NQWMI and UA)	107	14.8	12.4–17.5	442	371–523
Other ischaemic heart disease	363	50.1	46.6–53.8	1,499	1,393–1,609
Non-ischaemic heart disease pain	166	22.6	19.7–25.8	686	589–771
Total of chest pain EMAs	724	-	-	2,990	-

Key: CI = confidence intervals; MI = myocardial infarction; NQWMI = non-Q-wave myocardial infarction; UA = unstable angina

Table 3. Number of ACS events without ST elevation observed during the study period and projected to a one-year period; and number (%) of high-risk events by risk stratification criterion

	Observed during 14-week study period	% of all ACS events	Projected to a 52-week period
Total ACS events without ST elevation	117	-	442
TnT value ≥ 0.05 µg/L	82	70	309
TnT value ≥ 0.1 µg/L	77	66	291
ST depression ≥ 0.1 mV in at least two leads	25	21	94

Key: ACS = acute coronary syndrome; TnT = troponin T

ST elevation required urgent in-patient referral to tertiary centres, and of those 10 had revascularisation procedures.

Within the subgroup of 117 events due to ACS without ST elevation, 82 (70%) had a TnT value ≥ 0.05 µg/L, 77 (66%) a TnT value of ≥ 0.1 µg/L and 25 (21%) had ST depression ≥ 1mV in at least two ECG leads (table 3). All patients with ST depression ≥ 1mV in at least two ECG leads also had a TnT value of ≥ 0.1 mg/L.

By extrapolation, during a year, 442 separate ACS events without ST elevation eligible for treatment with GP IIb/IIIa inhibitors would be expected to occur in our hospital (table 3), translating to one ACS event for every 25.6 (CI 23.8–28.6) hospital EMAs. Using a theoretical 'catchment' population as a denominator, this represents an incidence of 147/100,000 population (95% CI 134–162).

Table 4. Cost of glycoprotein IIb/IIIa inhibitor treatment, by risk stratification (treatment eligibility) criterion used

Treatment criterion	Expected number of events per year (% total ACS events)	Cost of treatment per year (£)	Cost of treatment/ all-cause hospital EMA (£)
Troponin T value ≥ 0.05 µg/L	309 (70%)	139,000	12.1
Troponin T value ≥ 0.1 µg/L	291 (66%)	131,000	11.45
ST segment depression ≥ 0.1 mV in ≥ 2 leads OR TnT ≥ 0.1 µg/L	291 (66%)	131,000	11.45

Cost analysis

The results of the study were used to estimate the prescribing cost of GP IIb/IIIa inhibitors for high-risk cases of ACS without ST elevation, by different risk stratification criteria.[3,9,10] Using TnT values of either ≥ 0.05 or ≥ 0.1 µg/L as criteria for treatment, the annual number of events would be 309 and 291 respectively (table 4); estimated treatment costs would be £139,000 and £131,000 respectively, or £12.10 and £11.45 per all-cause hospital EMA. Using either ST segment depression ≥ 0.1 mV in at least two leads or a TnT value of ≥ 0.1 µg/L as the treatment criterion, the number of events and the cost would remain the same as for using a TnT value of ≥ 0.1 µg/L – all patients with significant ST depression also had TnT values ≥ 0.1 µg/L (table 3).

Discussion

These findings provide further evidence of the magnitude of the problem caused by patients presenting with acute chest pain likely to be due to cardiac causes in British hospitals.[1,2,11] In this survey these patients represented 22% of all EMAs. The results also provide an estimate of the disease burden of ACS without ST elevation and other chest pain presentations in relation to EMA activity in a typical general hospital. The observed frequency of ACS without ST elevation was 34% less than that expected using the NICE estimate of 230 ACS episodes/100,000 population.[3]

Evidence supports the use of GPIIb/IIIa inhibitors in high-risk patients with ACS without ST elevation: an elevated troponin level is the single most important predictive marker of high risk.[3,5] Data presented here could aid the estimation of prescribing costs relating to GPIIb/IIIa inhibitor treatment in other hospitals. The final cost, however, could vary according to the risk stratification and treatment eligibility criteria used.

Although ST depression on the admission ECG is not necessarily a marker for troponin positivity, all patients in our study with ST depression ≥ 0.1 mV in more than two leads were subsequently shown to have raised troponin levels. Troponin elevation remains the most useful method of risk stratification, and hospitals that do not have access to troponin measurement will substantially underestimate the high-risk group of ACS patients without ST elevation (table 3). However, the presence of ST

Key messages

- Between 20% and 30% of all emergency medical admissions (EMAs) are due to chest pain
- GPIIb/IIIa treatment is recommended by NICE for the treatment of high-risk patients with ACS without ST segment elevation
- One event of ACS without ST elevation should be expected for every 25.6 emergency medical admissions
- Using abnormal TnT values to define high-risk status, about two-thirds of all patients with ACS without ST elevation should be expected to be treated with GPIIb/IIIa inhibitors
- The annual cost of treatment could be estimated at about £12 per hospital EMA due to all causes

depression $\geq$ 0.1 mV in more than two leads allows the definition of a patient subgroup eligible for immediate treatment with GPIIb/IIIa inhibitors.

People from the theoretical catchment area of Stepping Hill Hospital may receive emergency treatment in other hospitals and vice versa, so it is difficult to calculate exact population incidence rates of ACS without ST elevation. In addition, some patients might have presented to the Accident & Emergency department with acute chest pain but not been admitted to a hospital bed and not been identified. However, by definition patients who are not admitted cannot receive treatment with GPIIb/IIIa inhibitors. The findings therefore provide a pragmatic estimate of the frequency of ACS in relation to the total number of EMAs and the cost of introducing GPIIb/IIIa inhibitor therapy in a typical district general hospital. Assessment of health need at a local level is important to help to define more accurately the cost implications of implementing national guidelines.

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