Excess of mortality in patients with chest pain peaks in the first 3 days period after the incident and normalizes after 1 month

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Background. Patients presenting with chest pain have a 5% chance of experiencing a coronary event. These patients are at risk of mortality and should be recognized and referred to secondary care.

Aim. To determine the relationship between referral type and mortality in patients with chest pain.

Methods. The design of the study is an observational study. The setting of the study is a sentinel network of general practices in Belgium, covering 1.6% of the total population. The subjects are 1558 consecutive patients consulting with chest pain in 2003. Descriptive analyses report the standardized mortality ratios. We used the Belgian population of 1999 as the reference population and as the standard population.

Results. The standardized mortality ratios of 3 days were 151.0 [95% confidence interval (CI): 82.3–250.3] for the urgent referred group, 45.5 (95% CI: 12.4–116.0) for non-urgent and 13.6 (95% CI: 1.7–49.4) for the non-referred group. The standardized ratios of 1 month were, respectively, 27.6 (95% CI: 18.0–40.4), 6.7 (95% CI: 2.5–14.6) and 4.7 (95% CI: 1.9–9.7). The standardized ratios of 2–12 months were normal for the urgent referral group (1.3; 95% CI: 0.7–2.2) and for the non-urgent referral group (1.0; 95% CI: 0.5–1.9) and even less in the non-referred group (0.4; 95% CI: 0.2–0.9).

Conclusions. Mortality in the first 3 days and first month after consulting for chest pain is very high. There is a marked trend in mortality according to the referral type—urgently referred, non-urgently referred and not referred—suggesting risk stratification by the GP. After 1 month, mortality normalizes for all groups, suggesting that the surviving patients are well treated and the condition causing the chest pain no longer influences survival compared to the general population.

Keywords. Chest pain, mortality rate, primary health care, referral and consultation, standardized ratios.

Background

In general practice, patients presenting with chest pain have a 5% chance of experiencing a coronary event. Chest pain can be a sign of an ischaemic or non-ischaemic cardiac disease, gastro-oesophageal, pulmonary and musculoskeletal disorders or a panic attack.

If chest pain is caused by an acute coronary syndrome, urgent referral to secondary care is imperative because mortality decreases if primary percutaneous coronary intervention (PCI) can be carried out quickly. Referring a large proportion of patients with chest pain to secondary care leads to unnecessary tests and procedures, with the related costs and complications. In addition, urgent referral may be contraindicated in some cases, for example, in patients suffering from a panic attack.

GPs thus need to decide whether they refer the patient with chest pain urgently by ambulance, not urgently by private transport or not at all. Previous studies have shown that this decision is influenced by the certitude of the initial diagnosis. The aim of this study was to determine the relationship between...
the referral decision—urgent, non-urgent or no referral—and the standardized mortality ratio in the first 12 months after the incident in patients consulting with chest pain.

Methods

The study was carried out in the Belgian sentinel network of general practices in 2003. This network was established 25 years ago as a voluntary and continuous registration of epidemiological data. The network consists of GPs from all regions of the country and is representative for the entire GP population with respect to gender and age. A detailed report of the method used to estimate the denominator in patient-years has been published elsewhere. At the time of this study, the network covered almost 1.6% of the Belgian population or 169 420 inhabitants. All patients consulting their GP with non-traumatic chest pain in 2003 were consecutively included in the study; details and results have been published previously. In September 2008, follow-up data on mortality were collected.

For this purpose, a letter was sent to all GPs of the sentinel network asking whether the patients included in the study were still alive or deceased and if deceased the exact date of death. Knowing the inclusion date, we were able to estimate in which survival category the deceased belonged; a reminder was sent 6 weeks later. GPs whose patient had died within 3 days after the incident and without urgent referral were asked for cause of death and reasons for the non-referral decision.

Mortality was categorized according to time after the incident: within 3 days, within a month, within 1 year and within 2–12 months. Referral decision was registered as no referral, non-urgent referral to specialist care and urgent referral to the emergency department.

Analyses

The relationship between the mortality rate and the referral type and the relationship between gender and mortality were bivariably analysed as proportions with their 95% confidence interval (CI). We concluded that the difference was statistically different when 95% CIs were not overlapping.

We compared mortality rates of our study groups with the mortality rates of the total Belgian population by calculating standardized mortality ratios, which compare the results in our study group with the results for the total Belgian population controlling for age and gender (indirect standardization). A standardized mortality ratio of 1 means that the mortality rate in this group is similar to the mortality rate in the Belgian population, controlled for age and gender. This also enabled us to compare mortality between groups, controlling for age and gender, as the results of all study groups were standardized for the same age and gender distribution (Table 2). All analyses were performed using Epi Info, version 3.2.21 and CIA version, 1.0.22

Results

Of the 163 GPs participating in the study, 140 (85.9%) provided follow-up information on 1558 (78.1%) of 1996 patients, 155 (7.8%) patients were not retrievable from the GP records, of which 118 were not referred at the time of the incident and 283 (14.2%) were missing because of the non-response of the GPs. The latter were found to be similar to the included patients in terms of age, gender and referral type.

One year after the incident, 69 patients had died, of which 20 within 3 days and 39 within 1 month (Table 1). The mortality rate in the urgent referred group was 5.8% within 3 days, 10.7% within 1 month and 16.1% within a year. By contrast, mortality in non-urgently referred and non-referred patients was 0.9% and 0.2% within 3 days, 1.4% and 0.8% within 1 month and 3.7% and 1.6% within 1 year, respectively. A chi-square for trend showed a significant trend over the referral categories for mortality within the first 3 days, within 1 month and within 1 year (P = 0.000 for each).

Standardized mortality ratios show that the excess mortality peaks in the first 3 days period, with urgently referred patients having a mortality of 151 times more than the Belgian population, non-urgent 45.5 times more and non-referred patients 13.6 times more (Table 2).

Mortality remains higher during the first month after the incident (ratios of 27.6, 6.7 and 4.7, respectively) but normalizes after 1 month for all referral groups. From our results, it appeared that non-referred group has a lower risk of death than the standardized Belgian population 1 month after the incident.

Six patients were not urgently referred at the time of the incident and died at home within 3 days. Their GPs stated that the patient refused hospitalization (five), signs and symptoms were unclear (two) and situation changed very quickly (one). One of those patients had severe chronic obstructive pulmonary disease and no specific cardiologic disease.

In the non-urgent referred group, patients who died within 1 month were younger than those in the two other groups (59 years compared to 81 years in the non-referred group and 80 in the urgent referred group) (Table 3). There was no difference with respect to gender between the three groups. However, numbers were small and differences statistically non-significant.

Discussion

Summary of the main findings

The mortality rates and standardized ratios varied according to referral type (urgent referral > non-urgent > no referral) and the time period (3 days > 1
They were very high within the first 3 days, especially for the urgently referred patients (ratio 151; rate 5.8%).

After the first month, mortality rates normalize for all referral types. In cases where a patient was not referred urgently and died within 3 days, patients refused urgent referral, presented with no or unclear signs and symptoms and experienced a quickly changing medical situation.

### Meaning of the results

Based on registration data of 2003, our results show that mortality risk is very high in the first 3 days period and high in the first month after an urgent referral for chest pain. This suggests that mortality due to acute coronary syndrome remains high, even in the invasive treatment period. More recent changes of primary PCI could produce better outcomes.

Mortality is much lower in the non-urgent and not referred group, suggesting that GPs perform a risk stratification in deciding who to refer and how. The reasons for not urgently referring the patients who died within 3 days are very familiar to all GPs, with the most frequent reason being patient refusal.

After the first month, the ratios are similar or even lower than the reference population. It could be that the surviving patients are well treated and the mortality after 1 month is no longer influenced by the condition causing chest pain. Deceased patients within a month

### Table 1 Mortality rates in chest pain patients by referral type

|                     | All patients $N = 1554$ | Non-referral, $N = 884$ | Non-urgent referral, $N = 428$ | Urgent referral, $N = 242$ |
|---------------------|-------------------------|-------------------------|-------------------------------|---------------------------|
| Within 3 days       | $n = 20$                | $n = 2$                 | $n = 4$                       | $n = 14$                  |
| % (95% CI)          | 1.3 (0.8–2.0)           | 0.2 (0.0–0.9)           | 0.9 (0.3–2.5)                 | 5.8 (3.2–9.5)             |
| Age (SD)            | 74.7 (13.6)             | 79.5 (0.7)              | 57.5 (16.6)                   | 78.9 (9.8)                |
| Within 1 month      | $n = 39$                | $n = 7$                 | $n = 6$                       | $n = 26$                  |
| % (95% CI)          | 2.5 (1.8–3.4)           | 0.8 (0.3–1.7)           | 1.4 (0.6–3.2)                 | 10.7 (7.1–15.3)           |
| Age (SD)            | 76.8 (11.6)             | 81.4 (5.7)              | 58.8 (13.3)                   | 79.7 (8.3)                |
| Within 1 year       | $n = 69$                | $n = 14$                | $n = 16$                      | $n = 39$                  |
| % (95% CI)          | 4.4 (3.5–5.6)           | 1.6 (0.9–2.7)           | 3.7 (2.2–6.1)                 | 16.1 (11.7–21.4)          |
| Age (SD)            | 76.9 (12.2)             | 75.0 (12.6)             | 70.0 (15.3)                   | 80.3 (9.2)                |
| 2–12 months         | $n = 30$                | $n = 7$                 | $n = 10$                      | $n = 13$                  |
| % (95% CI)          | 1.9 (1.3–2.5)           | 0.8 (0.3–1.7)           | 2.3 (1.4–3.2)                 | 5.5 (4.6–6.1)             |
| Age (SD)            | 76.9 (13.1)             | 68.6 (14.6)             | 76.7 (12.6)                   | 81.5 (11.2)               |

### Table 2 Standardized mortality ratio in chest pain patients

|                     | All patients | Non-referral | Non-urgent referral | Urgent referral |
|---------------------|--------------|--------------|---------------------|-----------------|
| Within 3 days (95% CI) | 61.0 (37.2–94.2) | 13.6 (1.7–49.4) | 45.5 (12.4–116.0) | 151.0 (82.3–250.3) |
| Within 1 month (95% CI) | 11.7 (8.3–16.0) | 4.7 (1.9–9.7) | 6.7 (2.5–14.6) | 27.6 (18.0–40.4) |
| Within 1 year (95% CI) | 1.7 (1.4–2.2) | 0.8 (0.4–1.3) | 1.5 (0.9–2.4) | 3.5 (2.5–4.7) |
| 2–12 months (95% CI) | 0.8 (0.5–1.2) | 0.4 (0.2–0.9) | 1.0 (0.5–1.9) | 1.3 (0.7–2.2) |

### Table 3 Age and gender of deceased patients

|                     | All patients | Non-referral | Non-urgent referral | Urgent referral |
|---------------------|--------------|--------------|---------------------|-----------------|
| Within 3 days       | Age (SD)     | 74.7 (13.6)  | 79.5 (0.7)          | 57.5 (16.6)     | 78.9 (9.8) |
| Male % (95% CI)     | 60 (36.1–80.9) | 50 (1.3–98.7) | 50 (1.3–98.7) | 64.3 (35.1–87.2) |
| Within 1 month      | Age (SD)     | 76.8 (11.6)  | 81.4 (5.7)          | 58.8 (13.3)     | 79.7 (8.3) |
| Male % (95% CI)     | 59.0 (42.1–74.4) | 42.9 (9.9–81.6) | 50.0 (11.8–88.2) | 65.4 (44.3–82.8) |
| Within 1 year       | Age (SD)     | 76.9 (12.2)  | 75.0 (12.6)         | 70.0 (15.3)     | 80.3 (9.2) |
| Male % (95% CI)     | 60.9 (48.4–72.4) | 64.3 (35.1–87.2) | 56.3 (29.9–80.2) | 61.5 (44.6–76.6) |
| 2–12 months         | Age (SD)     | 76.9 (13.1)  | 68.6 (14.6)         | 76.7 (12.6)     | 81.54 (11.2) |
| Male % (95% CI)     | 63.3 (43.9–80.1) | 85.7 (42.1–99.6) | 60.0 (26.2–87.8) | 53.8 (25.1–80.8) |
of the non-urgent referred group were younger (59 years) than in the other groups (80 and 81 years), but the number of cases (six) is too low to draw any firm conclusions.

**Strengths and weaknesses of the study**

There is no significant difference between the non-urgent referred group versus the two other groups (non-referred group or the urgent referred group) for the 3 days period. There is a significant difference, however, between the non-referred and the urgent referred groups. Because of the relatively small number of events, the 95% CI, especially for the mortality within 3 days, are very wide. So these results should be interpreted with caution.

To our knowledge, this is the first study exploring the relationship between referral decisions and mortality carried out in a general practice setting. The long-standing experience of the Belgian network of sentinel practices made it possible to include a large number of patients. Receiving follow-up information on 86% of the patients illustrates the enthusiasm and seriousness of the sentinel network’s members.

However, information could not be retrieved from 7.8% of patients as a result of the GP’s individual reference system to his or her medical records. Most missing patients were non-referred patients, who were the youngest and healthiest, probably rarely consulting the GP. This is also the reason why the mortality ratios may have been slightly overestimated because more information about the non-referred patients (with the lowest mortality) is missing than from the other groups. Assuming that there were no deceased patients in the missing group, the 1-month mortality rate will change from 0.8% to 0.6% for the non-referred group, from 1.4% to 1.2% for the non-urgent referred group and from 10.7% to 8.6% for the urgent referred group. On the other hand, assuming that all patients from the missing data group died, the 1-month mortality rate will change to 25.9%, 17.9% and 27.2%, respectively.

We do not have a final diagnosis for the non-referred patients, in whom acute coronary may be a minor event and may even go undetected.23 But, since this study was designed to evaluate mortality, it does not affect our conclusions.

**Previous studies**

Comparison with other studies is difficult as most were performed in a hospital setting including only acute coronary patients or acute myocardial infarction patients, whereas we included an initially unselected group of non-traumatic patients with chest pain.

In a systematic review of patients with angina recruited within primary care, an annual mortality rate of 2.8–6.6 was found, which is similar to our results (4.4% in 1 year).24 In contrast in patients with an acute coronary syndrome in Finland, the 10-month mortality rate was 19% for patients with ST-elevation myocardial infarction, 27% for patients without ST-elevation myocardial infarction and 12% for patients with unstable angina, all of which are markedly higher than the rates found in our study.25 To put our mortality rates more in context, we underpin that in another part of our observational study, 122 (41%) of the 297 patients who were urgently referred had a final diagnosis of acute coronary syndrome.18

**Future research**

Our present study has yielded some hypotheses that could be further investigated in future studies. The marked trend in mortality between urgent referred, non-urgent referred and non-referred groups suggests that GPs stratify the risk for immediate mortality. However, it is not always clear which threshold they use to refer a patient with chest pain and what influences this threshold.

Moreover, the question as to their preference for urgent or non-urgent referral is as yet unresolved. A qualitative study could help to explore this. Secondly, although the mortality in non-urgent referred and non-referred patients was lower than that in the urgent referred group, these patients do experience an increased risk for immediate mortality compared to the general population. A new study with registration of all final diagnoses will allow further research on risk factors for immediate mortality and incorporate these in the referral decisions in the future.

**Conclusions**

Based on data from 2003, mortality in the first 3 days period and the first month after consulting for chest pain is very high. There is a marked trend in mortality according to the referral type—urgent referred, non-urgent referred and not referred—suggesting risk stratification by the GP. After 1 month, mortality normalizes for all groups, suggesting that the surviving patients are well treated and the condition causing the chest pain no longer influences survival compared to the general population.

**What is already known on this subject**

In general practice, patients presenting with chest pain have a 5% chance of having a coronary event. Patients with acute coronary syndrome are at risk of mortality and as such should be recognized and referred to secondary care.

**What this study adds**

Mortality in the first 3 days period and first month after consulting for chest pain is very high. After 1 month,
mortality normalizes suggesting that the surviving patients are well treated and the condition causing the chest pain no longer influences survival compared to the general population.

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Authors’ contributions: RB, AV, FB and BA designed the study. VV was responsible for collecting the data. RB and BA analysed the data. RB wrote the first draft of the article. FB, AV and BA provided substantial subsequent contributions as did VV for the final draft. BA supervised the study design and analysis. RB is guarantor.

Declaration

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