

Prevalence of and risk factors for persistent postoperative nonanginal pain after cardiac surgery: a 2-year prospective multicentre study

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ABSTRACT

Background: Persistent postoperative pain continues to be an underrecognized complication. We examined the prevalence of and risk factors for this type of pain after cardiac surgery.

Methods: We enrolled patients scheduled for coronary artery bypass grafting or valve replacement, or both, from Feb. 8, 2005, to Sept. 1, 2009. Validated measures were used to assess (a) preoperative anxiety and depression, tendency to catastrophize in the face of pain, health-related quality of life and presence of persistent pain; (b) pain intensity and interference in the first postoperative week; and (c) presence and intensity of persistent postoperative pain at 3, 6, 12 and 24 months after surgery. The primary outcome was the presence of persistent postoperative pain during 24 months of follow-up.

Results: A total of 1247 patients completed the preoperative assessment. Follow-up retention rates at 3 and 24 months were 84% and 78%, respectively. The prevalence of persis-

tent postoperative pain decreased significantly over time, from 40.1% at 3 months to 22.1% at 6 months, 16.5% at 12 months and 9.5% at 24 months; the pain was rated as moderate to severe in 3.6% at 24 months. Acute postoperative pain predicted both the presence and severity of persistent postoperative pain. The more intense the pain during the first week after surgery and the more it interfered with functioning, the more likely the patients were to report persistent postoperative pain. Pre-existing persistent pain and increased preoperative anxiety also predicted the presence of persistent postoperative pain.

Interpretation: Persistent postoperative pain of nonanginal origin after cardiac surgery affected a substantial proportion of the study population. Future research is needed to determine whether interventions to modify certain risk factors, such as preoperative anxiety and the severity of pain before and immediately after surgery, may help to minimize or prevent persistent postoperative pain.

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Postoperative pain that persists beyond the normal time for tissue healing (> 3 mo) is increasingly recognized as an important complication after various types of surgery and can have serious consequences on patients' daily living.¹⁻³ Cardiac surgeries, such as coronary artery bypass grafting (CABG) and valve replacement, rank among the most frequently performed interventions worldwide.⁴ They aim to improve survival and quality of life by reducing symptoms, including anginal pain. However, persistent postoperative pain of nonanginal origin has been reported in 7% to 60% of patients following these surgeries.⁵⁻²³ Such variability is common in other types of major

surgery and is due mainly to differences in the definition of persistent postoperative pain, study design, data collection methods and duration of follow-up.^{1-3,24}

Few prospective cohort studies have examined the exact time course of persistent postoperative pain after cardiac surgery, and follow-up has always been limited to a year or less.^{9,14,25} Factors that put patients at risk of this type of problem are poorly understood.²⁶ Studies have reported inconsistent results regarding the contribution of age, sex, body mass index, preoperative angina, surgical technique, grafting site, postoperative complications or level of opioid consumption after surgery.^{5-7,9,13,14,16-19,21-23,25,27} Only

1 study investigated the role of chronic nonanginal pain before surgery as a contributing factor;²¹ 5 others prospectively assessed the association between persistent postoperative pain and acute pain intensity in the first postoperative week but reported conflicting results.^{13,14,21,22,25} All of the above studies were carried out in a single hospital and included relatively small samples. None of the studies examined the contribution of psychological factors such as levels of anxiety and depression before cardiac surgery, although these factors have been shown to influence acute or persistent postoperative pain in other types of surgery.^{1,24,28,29}

We conducted a prospective multicentre cohort study (the CARD-PAIN study) to determine the prevalence of persistent postoperative pain of nonanginal origin up to 24 months after cardiac surgery and to identify risk factors for the presence and severity of the condition.

Methods

Study design and population

We carried out an observational prospective study involving a large cohort of patients undergoing cardiac surgery from Feb. 8, 2005, to Sept. 1, 2009, and followed up for 24 months. Recruitment took place in 4 Canadian university-affiliated cardiac surgery centres (the Montreal Heart Institute, the Peter Munk Cardiac Centre, the Institut universitaire de cardiologie et de pneumologie de Québec and the Maritime Heart Center). The study was approved by the research ethics board of each institution.

Experienced research assistants (nurses or respiratory therapists) screened patients for study eligibility in the preadmission clinic in the 4 weeks before surgery. Patients were included if they were 18 years or older; they were undergoing elective CABG or valve replacement, or both, via median sternotomy for the first time; and they had never undergone thoracotomy or mastectomy. They were excluded if they could not complete the questionnaires because of physical or mental incapacity or had insufficient knowledge of French or English.

Data collection

All consenting participants took part in a structured interview conducted by the research nurses or respiratory therapists. Patient demographics and body mass index were recorded in addition to the following study measures, all of which had well-established validity and reliability. The Canadian Cardiovascular Society grading scale³⁰ was used to document the severity of preoperative angina in terms of physical limitations. The

presence of persistent nonanginal pain (e.g., migraine, arthritic pain) for at least 3 months before surgery was also assessed. Because pain involves not only a biological component but also important emotional and cognitive dimensions, the Hospital Anxiety and Depression Scale³¹ was used to measure patients' anxiety and depression levels. The Pain Catastrophizing Scale³² was used to assess patients' negative cognitive-affective responses to pain. Finally, the SF-12v2 Health Survey³³ was used to assess preoperative physical and mental health-related quality of life.

Data collection during the hospital stay and at follow-up (at 3, 6, 12 and 24 months) was done by the research nurses and respiratory therapists involved in patient recruitment and initial interviews. In some study sites, additional research assistants (graduate students) were hired to collect data on weekends or during evenings. All efforts were made to ensure uniformity of the procedures at each site (e.g., standardized comprehensive training by one person [the research nurse coordinator], use of a structured face-to-face interview protocol to collect perioperative data across the study sites and use of a structured telephone interview protocol at follow-up in all sites).

At 24, 48 and 72 hours and 7 days after surgery, patients were asked to rate the intensity of their worst and average postoperative pain on movement during the preceding 24 hours using a standard numerical rating scale (0 = no pain, 10 = worst possible pain).³⁴ On day 7, the pain interference items of the Brief Pain Inventory were administered to evaluate the extent to which patients' pain was interfering with their general activity, mood, walking, work, relations with others, sleep and enjoyment of life (0 = does not interfere, 10 = completely interferes).³⁵ We added 3 items to this assessment: deep breathing or coughing, appetite and concentration. A total score was calculated from the sum of all the items. Participants discharged home before day 7 were telephoned to collect their pain ratings and interference scores.

The following medical and surgical data during the hospital stays were extracted from patient charts by the research nurses: type and duration of surgery, postoperative complications, length of stay in the intensive care unit (ICU), time in hospital after discharge from the ICU and use of analgesic medications. Total doses of opioids from day 1 to 7 were converted into milligrams of parenteral morphine equivalents.

At 3, 6, 12 and 24 months after surgery, patients were interviewed by telephone to measure the presence of persistent postoperative pain

using a structured interview protocol. Pain was defined as persistent postoperative pain if it met the following 3 criteria: it first appeared after surgery; it was not related to pain felt before surgery (e.g., anginal pain) or to other causes (e.g., infection); and it was present for at least 3 months.³ Patients who met all 3 criteria were asked to rate the intensity of their average pain in the past 7 days using the numerical rating scale (0 = no pain, 10 = worst possible pain).³⁴

Outcome measures

The primary outcome was the presence of persistent postoperative pain during 24 months of follow-up. The secondary outcome was the severity of this type of pain in terms of intensity on the numerical rating scale.

Statistical analysis

As in previous studies in the cardiac surgery field,^{9,14,19,22,36} we defined acute and persistent post-

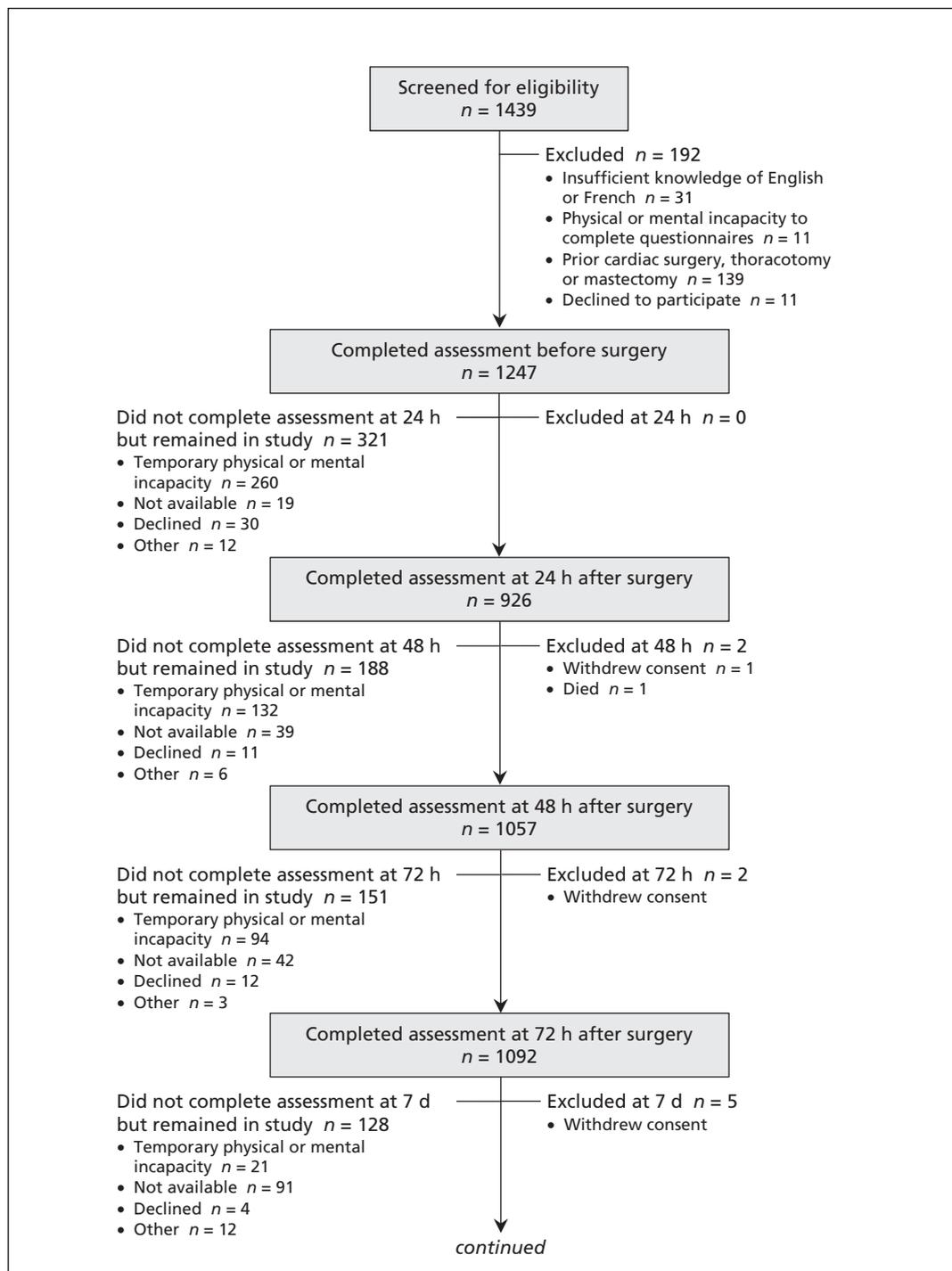


Figure 1 (part 1 of 2): Study flow.

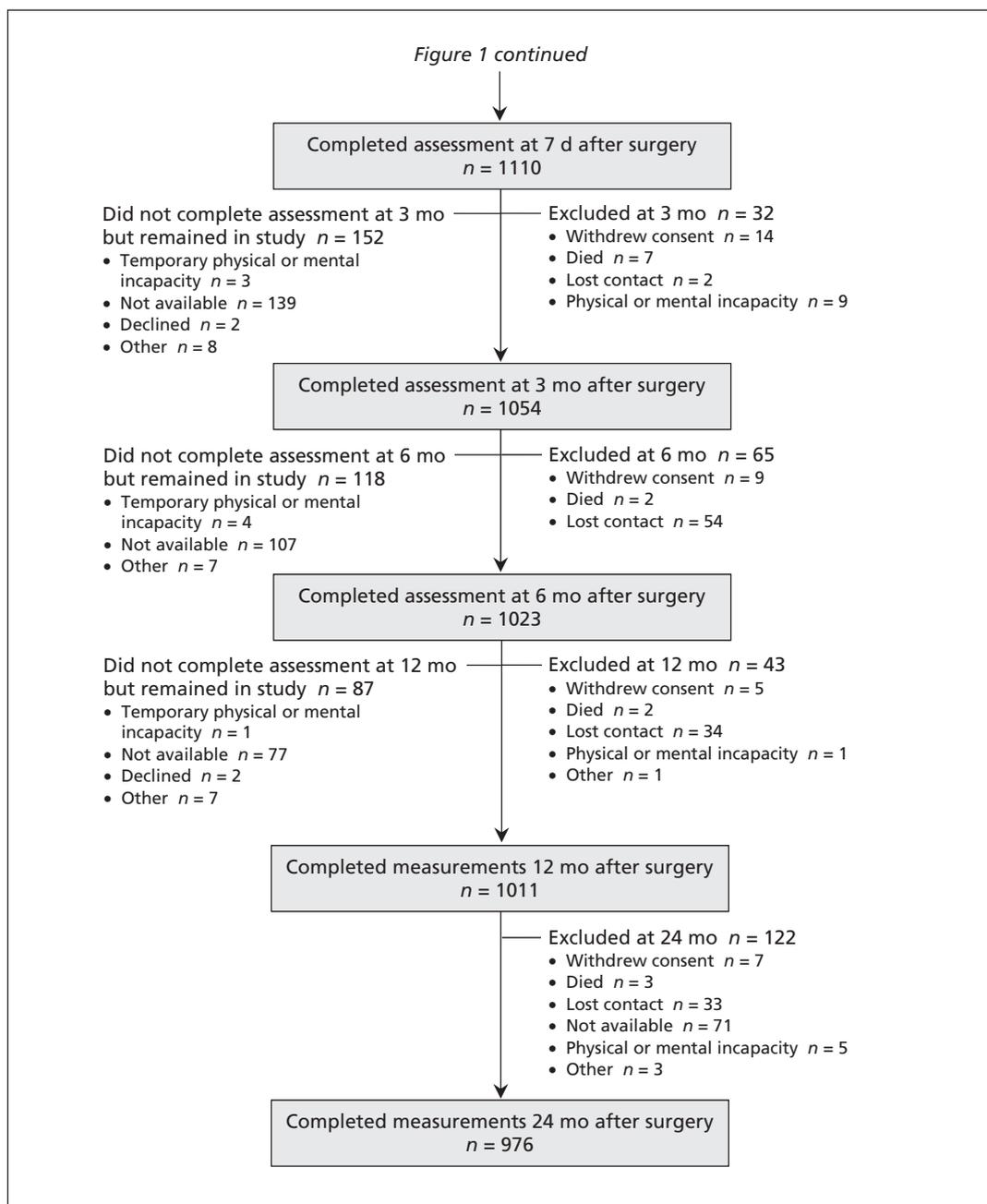


Figure 1 (part 2 of 2): Study flow.

operative pain as moderate to severe if the patient reported a pain intensity score of 4 or higher out of 10 on the numerical rating scale.

To identify participant characteristics related to persistent postoperative pain over time, we used generalized estimating equation (GEE) models for binary outcomes, which provide robust estimates while adjusting for lack of independence due to sampling of multiple observations per patient and multiple patients from the same study site.³⁷ In the models, we included only patients for whom data were available on demographic information and preoperative measurements, pain ratings on postoperative day 3

(when increased ambulation usually results in peak pain levels³⁶), pain interference scores on day 7 and information from at least 1 follow-up interview at 3, 6, 12 or 24 months after surgery. All available data on patients meeting inclusion criteria were used in the models regardless if 1 to 3 follow-up interviews were missing. There was no imputation for missing data or time points.

The models examined the effects of each potential predictor, time and the interaction between the variables and time. Variables or interaction terms significant at a *p* value of 0.10 or less were included in the multivariable models. Collinear variables were identified, and the

variable with the smaller effect size was omitted from the multivariable equation.

Model fit and covariance structure were assessed with use of the QIC (quasi-likelihood under independence model criterion) statistic and regression diagnostics (e.g., standardized Pearson residuals, leverages, changes in deviance).

Results

A total of 1247 patients were enrolled, and 976 (78.3%) of them were available for follow-up 24 months after surgery (Figure 1). A total of 975 patients (78.2%) who participated in the preoperative interview were included in the GEE models because they also provided the requisite postoperative measures and completed at least 1 follow-up interview at 3, 6, 12 or 24 months after surgery. Most of the 975 patients were men (79.0%) and underwent CABG with or without valve replacement (76.6%); the mean age was 61.9 (range 21–86) years (Table 1).

The proportion of all participants who rated their worst pain on movement during the preceding 24 hours as moderate to severe remained above 65% across all time points in the first week after surgery (Table 2, Figure 2). A substantial proportion of participants also rated their average 24-hour pain on movement as moderate to severe at the same time points; the proportion was 43% on day 7.

Of the patients who completed assessments at each follow-up point, 40.1% reported experiencing persistent postoperative pain of any intensity (> 0 out of 10) 3 months after surgery. The proportion decreased significantly over time ($p < 0.001$): it was relatively stable at 6 months (22.1%) and 12 months (16.5%) and then reached 9.5% at 24 months (Table 3, Figure 3). When taking pain intensity into account, the prevalence of moderate to severe persistent postoperative pain in the 7 days before the follow-up interview also declined over time ($p < 0.001$), from 14.1% at 3 months to 3.6% at 24 months (Table 3, Figure 3).

In the multivariable GEE regression model, factors that emerged as significant independent predictors of persistent postoperative pain of any intensity were young age, persistent nonanginal pain before surgery, anxiety before surgery, moderate to severe acute pain on the third postoperative day and increased interference of the pain with various aspects of daily living 1 week after surgery (Table 4). A significant negative association was found between duration of surgery and persistent postoperative pain.

When we used the GEE model to examine

predictors of persistent postoperative pain of moderate to severe intensity, the only ones similar to predictors of any persistent postoperative pain were moderate to severe acute pain on the third postoperative day (adjusted odds ratio [OR] 2.67, 95% confidence interval [CI] 1.74–4.11) and the pain's interference with various aspects of daily living 1 week after surgery (OR 1.03, 95% CI 1.02–1.04) (Table 5). Sex but not age was a significant independent predictor, with women being more likely than men to report persistent postoperative pain of moderate to severe intensity

Table 1: Characteristics of patients with persistent postoperative pain of nonanginal origin following cardiac surgery ($n = 975^*$)

Characteristic	Mean \pm SD or no. (%) of patients*
Age, yr	61.9 \pm 10.2
Sex, male	770 (79.0)
Education level	
Elementary school	150 (15.4)
High school	348 (35.7)
College or technical school	245 (25.1)
University	232 (23.8)
Body mass index	28.7 \pm 4.8
CCS grading of angina†	
Class I	74 (7.6)
Class II	293 (30.1)
Class III	182 (18.7)
Class IV	63 (6.5)
NA	363 (37.2)
Persistent nonanginal pain before surgery	
Yes	326 (33.4)
No	649 (66.6)
Types of surgery	
CABG alone	640 (65.6)
Valve replacement alone	228 (23.4)
CABG and valve replacement	107 (11.0)
Postoperative complications	
Yes	541 (55.5)
No	434 (44.5)
Duration of surgery, h	3.4 \pm 1.0
Time in ICU, d	1.4 \pm 1.0
Time in hospital after discharge from ICU, d	5.2 \pm 2.7
Total dose of opioids during first wk after surgery, mg‡	98.5 \pm 63.0

Note: CABG = coronary artery bypass grafting, CCS = Canadian Cardiovascular Society, ICU = intensive care unit, NA = not applicable, SD = standard deviation.

*Only the 975 patients whose data were included in the regression analyses are represented in this table (i.e., those who provided demographic information, preoperative pain measurements, pain ratings on postoperative day 3, pain interference scores on day 7, and at least 1 follow-up interview at 3, 6, 12 or 24 mo after surgery).

†Class I = angina only during strenuous or prolonged physical activity; class II = angina only during vigorous physical activity; class III = symptoms with everyday living activities; class IV = inability to perform any activity without angina, or angina at rest.

‡Expressed in milligrams of parenteral morphine equivalents.

at all follow-up times (adjusted OR 1.62, 95% CI 1.11–2.35). A significant association was found between time spent in the ICU and persistent postoperative pain severity (adjusted OR 1.19, 95% CI 1.05–1.36). A significant negative association was found between time spent in hospital after the ICU and persistent pain: the longer the stay in hospital after discharge from the ICU, the less likely patients were to report moderate to severe persistent postoperative pain (adjusted OR 0.86, 95% CI 0.78–0.95).

Interpretation

In our study, 9.5% of participants experienced persistent postoperative pain at 24 months after surgery. This proportion decreased to 3.6% when pain of moderate to severe intensity was considered. Results at earlier follow-up points are con-

sistent with those reported in several prospective studies of shorter duration among cardiac surgery patients.^{9,13,14,20,21,25}

These prevalence rates are not negligible given that more than 400 000 patients undergo CABG annually in the United States⁴ and that persistent postoperative pain affects patients' health-related quality of life.^{7–9,19} The risk of persistent postoperative pain should be discussed with patients during preoperative counselling and perhaps included in informed consent for surgery.^{3,38} Surgeons and cardiologists need to assess the presence and severity of persistent postoperative pain at follow-up visits. Patients may not mention their pain because attention is focused on their cardiac condition. Clinicians' lack of familiarity with the prevalence or potential treatments of persistent postoperative pain may result in no or deficient pain management.²⁶

Consistent with observations made in cardiac^{14,22} and noncardiac surgery patient cohorts,^{1–3,24} we showed that the intensity of acute postoperative pain was a significant predictor of both the presence and the severity of persistent postoperative pain. Irrespective of study sites, patients with higher ratings for acute pain and interference with daily functioning in the first week after surgery were more likely to report persistent postoperative pain at 24 months.

That pain can predict later pain is further illustrated by our finding that patients who had chronic nonanginal pain before surgery were at significantly increased risk of persistent postoperative pain. This result is consistent with those from reports in noncardiac surgery cohorts^{1–3,24} and suggests the manifestation of some predisposing factors. However, it is unknown whether the development of persistent postoperative pain is causally linked to the presence of pre-existing chronic pain or the severity of acute postoperative pain (e.g., by central sensitization or development of a pain memory), or whether this link is simply associative (i.e., they all are influenced by similar risk factors, such as genetic determinants).^{1–3,24} The literature on the prevention of persistent postoperative pain through the provision of adequate acute pain relief does not really shed light on this issue, despite encouraging results for some surgical interventions.³⁹ In cardiac surgery, the evidence to support any protective analgesic regimen is either lacking or limited.²⁶

Other factors that predicted either the presence or severity of persistent postoperative pain included age and sex, a result that is consistent with earlier observations in cardiac surgery cohorts.^{7,9,12,18,21,22} Increased anxiety before surgery

Table 2: Proportion of patients who rated their worst and average pain on movement during the previous 24 h as moderate to severe* in the first week after surgery

Time after surgery	Pain rated as moderate to severe; % (no.) of patients†	
	Worst	Average
24 h	85.0 (787/926)	64.0 (593/926)
48 h	86.0 (909/1057)	68.0 (719/1057)
72 h	74.0 (808/1092)	54.0 (590/1092)
Day 7	65.0 (722/1110)	43.0 (477/1110)

*Rating ≥ 4 out of 10 on standard numerical rating scale.
†Data for patients who completed the pain measurements at each point are shown.

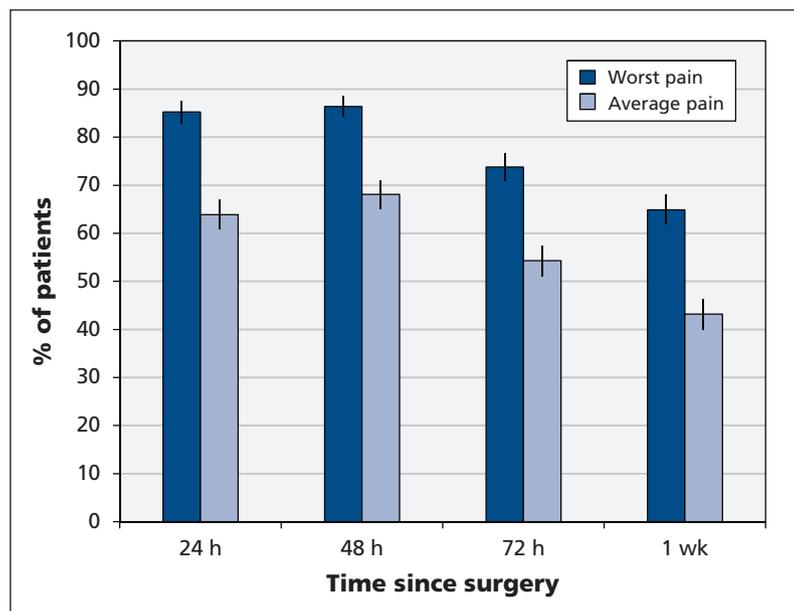


Figure 2: Proportion of patients who rated their worst and average pain on movement during the previous 24 hours as moderate to severe in the first week after surgery. Error bars represent 95% confidence intervals.

was also found to be a significant risk factor whose association with persistent postoperative pain was independent of its influence on acute postoperative pain. Assessment of anxiety levels before cardiac surgery may be beneficial, because psychological counselling, education and medical treatment, alone or in combination, may help to improve long-term outcomes of targeted patients.

As reported in previous studies,^{9,17,19,21,25,35} we found no significant association between the type of surgery (CABG or valve replacement, or both) and persistent postoperative pain. However, we found that the longer the surgery lasted, the less likely patients were to report any persistent postoperative pain. This finding was unexpected, and we have no explanation for it. Reviews of the existing literature on other types of surgery^{1-3,24} suggest an association in the opposite direction, if any. However, the studies we retrieved in the field of cardiac surgery failed to find an association between duration of the operation and persistent postoperative pain.

The length of time spent in the ICU did not predict the presence of persistent postoperative pain, but it did help to distinguish patients with moderate to severe pain from those with no or mild pain. We found a significant negative association between length of hospital stay after ICU discharge and intensity of persistent postoperative pain. It is tempting to speculate that patients who were discharged from ICU earlier were provided with insufficient analgesia and experienced more pain at home, which may have increased their risk of more intense persistent postoperative pain.

Strengths and limitations

Our study has several strengths. It was a prospective, multicentre study with a large cohort of cardiac surgery patients. Also, the follow-up was 24 months after surgery, as compared with 12 months or less in earlier studies.^{9,14,25}

Detailed neurophysiological examinations and quantitative sensory testing were not performed to assess the presence of sensory abnormalities in the area of surgery (e.g., hyperesthesia, hypoesthesia) in the pre- and postoperative periods. Therefore, we were unable to evaluate the potential role of altered pain processing due to intraoperative nerve injury or to some general predispositional factors in the development of persistent postoperative pain.^{1-3,24} Another limitation is that our results are based on self-reported pain. However, we applied rigorous definition criteria of persistent postoperative pain,³ and great care

was taken to exclude the possibility that pain was continuing from a pre-existing problem including angina.

Conclusion

Persistent postoperative pain of nonanginal origin was experienced by about 10% of patients after cardiac surgery, and moderate to severe pain by about 4%. Given the impact such pain may have on daily functioning and quality of life, patients should be informed about this possibility. We identified several significant risk factors of persistent postoperative pain, including 2 that can be managed (increased anxiety before surgery and acute postoperative pain in the first week after surgery). The severity of persistent preoperative pain may also be amenable to change. Future research should evaluate the

Table 3: Proportion of patients who reported experiencing any persistent postoperative pain and persistent pain of moderate to severe intensity* up to 24 mo after surgery

Time after surgery, mo	Persistent postoperative pain; % (no.) of patients†	
	Any	Moderate to severe
3	40.1 (423/1054)	14.1 (149/1054)
6	22.1 (226/1023)	7.0 (72/1023)
12	16.5 (167/1011)	6.6 (67/1011)
24	9.5 (93/976)	3.6 (35/976)

*Rating ≥ 4 out of 10 on standard numerical rating scale.
†Data for patients who completed the pain measurements at each point are shown.

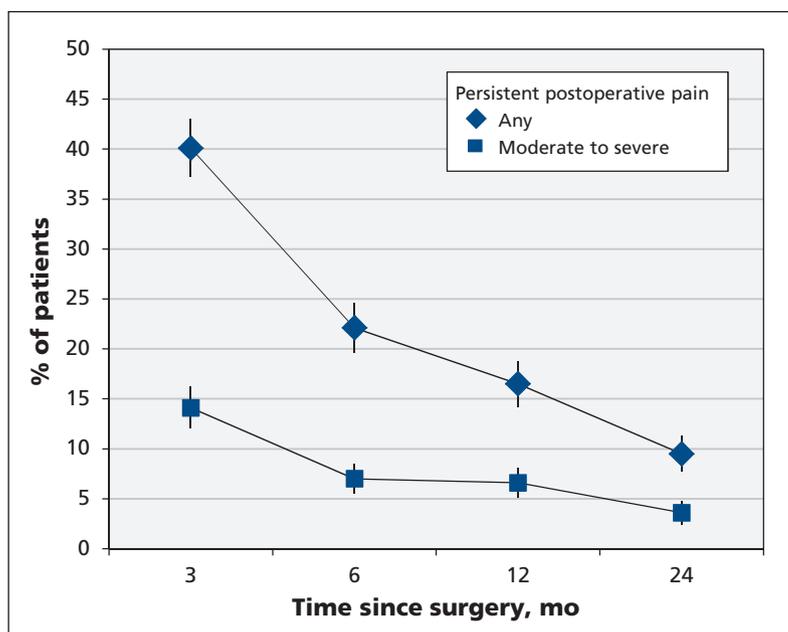


Figure 3: Proportion of patients who reported experiencing persistent postoperative pain up to 24 months after surgery. Error bars represent 95% confidence intervals.

Table 4: Results of generalized estimating equation (logit) regression analyses to predict presence of any persistent postoperative nonanginal pain over time ($n = 975^*$)

Variable	Crude OR (95% CI)	Adjusted OR† (95% CI)
Potential predictors before surgery		
Female sex	1.61 (1.26–2.07)	1.13 (0.85–1.50)
Age group, yr (v. ≥ 76 yr)		
21–55	2.51 (1.64–3.83)	1.87 (1.09–3.19)
56–65	1.90 (1.27–2.85)	1.43 (0.85–2.41)
66–75	1.57 (1.00–2.40)	1.28 (0.76–2.15)
Education level (v. university)		
Elementary school	0.98 (0.70–1.39)	–
High school	0.92 (0.69–1.22)	–
College or technical school	0.90 (0.66–1.22)	–
Body mass index, continuous	1.02 (0.99–1.04)	–
CCS grading scale of angina (v. class I)‡		
Class II	0.76 (0.50–1.16)	–
Class III	0.75 (0.48–1.16)	–
Class IV	1.58 (0.93–2.68)	–
NA	0.71 (0.47–1.08)	–
Persistent nonanginal pain before surgery (v. none)	1.57 (1.26–1.96)	1.44 (1.12–1.86)
HADS Anxiety, continuous	1.09 (1.06–1.11)	1.04 (1.00–1.09)
HADS Depression, continuous	1.06 (1.03–1.10)	0.98 (0.93–1.04)
Pain Catastrophizing Scale score, continuous	1.02 (1.01–1.03)	1.00 (0.99–1.02)
SF-12v2 mental health summary score, continuous	0.95 (0.93–0.97)	1.02 (0.98–1.07)
SF-12v2 physical health summary score, continuous	0.95 (0.92–0.97)	0.99 (0.95–1.02)
Potential predictors during or after surgery		
Type of surgery (v. CABG and valve replacement)		
CABG alone	1.14 (0.79–1.64)	–
Valve replacement alone	1.24 (0.83–1.85)	–
Duration of surgery, h, continuous	0.84 (0.75–0.94)	0.85 (0.75–0.96)
Time in ICU, d, continuous	1.03 (0.96–1.11)	–
Time in hospital after discharge from ICU, d, continuous	0.95 (0.91–1.00)	0.95 (0.90–1.01)
Postoperative complications (v. none)	0.86 (0.69–1.06)	–
Average pain in previous 24 h rated as moderate to severe§ on day 3 after surgery (v. none)	2.23 (1.78–2.79)	1.48 (1.10–2.00)
Worst pain in previous 24 h rated as moderate to severe§ on day 3 after surgery (v. none)	2.58 (1.94–3.44)	1.69 (1.16–2.47)
Total BPI pain interference score on day 7 after surgery, continuous	1.04 (1.03–1.05)	1.03 (1.02–1.04)
Total dose of opioids¶ administered during first wk after surgery, continuous per 10-unit dose	1.02 (1.00–1.04)	1.00 (1.00–1.00)
<p>Note: BPI = Brief Pain Inventory, CABG = coronary artery bypass grafting, CCS = Canadian Cardiovascular Society, CI = confidence interval, HADS = Hospital Anxiety and Depression Scale, ICU = intensive care unit, NA = not applicable, OR = odds ratio.</p> <p>*Data are included only for the 975 patients who provided demographic information, preoperative pain measurements, pain ratings on postoperative day 3, pain interference scores on day 7, and at least 1 follow-up interview at 3, 6, 12 or 24 mo after surgery.</p> <p>†Adjusted for sex, age group, persistent nonanginal pain before surgery, HADS anxiety and depression scores, Pain Catastrophizing Scale score, SF-12v2 mental and physical health summary scores, duration of surgery, time in hospital after discharge from ICU, average pain in previous 24 h, worst pain in previous 24 h, BPI pain interference score on day 7 and total opioid use.</p> <p>‡Class I = angina only during strenuous or prolonged physical activity; class II = angina only during vigorous physical activity; class III = symptoms with everyday living activities; class IV = inability to perform any activity without angina, or angina at rest.</p> <p>§Rating ≥ 4 out of 10 on standard numerical rating scale.</p> <p>¶Expressed as milligrams of parenteral morphine equivalents.</p>		

Table 5: Results of generalized estimating equation (logit) regression analyses to predict persistent postoperative nonanginal pain of moderate to severe intensity over time ($n = 975^*$)

Variable	Crude OR (95% CI)	Adjusted OR† (95% CI)
Potential predictors before surgery		
Female sex	2.09 (1.50–2.91)	1.62 (1.11–2.35)
Age group, yr (v. ≥ 76 yr)		
21–55	1.97 (1.00–3.89)	–
56–65	1.71 (0.88–3.31)	–
66–75	1.33 (0.68–2.63)	–
Education level (v. university)		
Elementary school	1.58 (0.94–2.64)	–
High school	1.29 (0.83–1.99)	–
College or technical school	0.94 (0.57–1.56)	–
Body mass index, continuous	1.02 (0.99–1.06)	–
CCS grading scale of angina (v. class I)‡		
Class II	1.35 (0.73–2.51)	1.08 (0.56–2.09)
Class III	1.67 (0.87–3.24)	1.32 (0.65–2.69)
Class IV	3.44 (1.67–7.08)	1.81 (0.83–3.92)
NA	1.17 (0.63–2.16)	1.03 (0.54–1.96)
Persistent nonanginal pain before surgery (v. none)	1.40 (1.01–1.94)	1.20 (0.85–1.71)
HADS Anxiety, continuous	1.11 (1.07–1.15)	1.04 (0.99–1.10)
HADS Depression, continuous	1.12 (1.07–1.16)	1.00 (0.92–1.07)
Pain Catastrophizing Scale score, continuous	1.04 (1.02–1.05)	1.01 (0.99–1.03)
SF-12v2 mental health summary score, continuous	0.91 (0.88–0.94)	0.98 (0.92–1.04)
SF-12v2 physical health summary score, continuous	0.90 (0.87–0.94)	0.97 (0.92–1.02)
Potential predictors during or after surgery		
Type of surgery (v. CABG and valve replacement)		
CABG alone	1.35 (0.80–2.28)	–
Valve replacement alone	1.25 (0.70–2.23)	–
Duration of surgery, h, continuous	0.88 (0.74–1.06)	–
Time in ICU, d, continuous	1.07 (0.99–1.14)	1.19 (1.05–1.36)
Time in hospital after discharge from ICU, d, continuous	0.88 (0.81–0.96)	0.86 (0.78–0.95)
Postoperative complications (v. none)	0.76 (0.56–1.05)	0.90 (0.62–1.30)
Average pain in previous 24 h rated as moderate to severe§ on day 3 after surgery (v. none)	3.92 (2.69–5.70)	2.67 (1.74–4.11)
Total BPI pain interference score on day 7 after surgery, continuous	1.04 (1.03–1.06)	1.03 (1.02–1.04)
Total dose of opioids¶ administered during first wk after surgery, continuous per 10-unit dose	1.02 (1.00–1.04)	1.00 (1.00–1.00)
<p>Note: BPI = Brief Pain Inventory, CABG = coronary artery bypass grafting, CCS = Canadian Cardiovascular Society, CI = confidence interval, HADS = Hospital Anxiety and Depression Scale, ICU = intensive care unit, NA = not applicable, OR = odds ratio.</p> <p>*Data are included only for the 975 patients who provided demographic information, preoperative pain measurements, pain ratings on postoperative day 3, pain interference scores on day 7, and at least one follow-up interview at 3, 6, 12 or 24 mo after surgery.</p> <p>†Adjusted for sex, CCS class, persistent nonanginal pain before surgery, HADS anxiety and depression scores, Pain Catastrophizing Scale score, SF-12v2 mental and physical health summary scores, time in ICU, time in hospital after discharge from ICU, average pain in previous 24 h, BPI pain interference score on day 7 and total opioid use.</p> <p>‡Class I = angina only during strenuous or prolonged physical activity; class II = angina only during vigorous physical activity; class III = symptoms with everyday living activities; class IV = inability to perform any activity without angina, or angina at rest.</p> <p>§Rating ≥ 4 out of 10 on standard numerical rating scale.</p> <p>¶Expressed as milligrams of parenteral morphine equivalents.</p>		

effects of such interventions in a balanced regimen of multimodal treatments. Well-designed, carefully controlled studies are needed to determine whether persistent postoperative pain can be minimized or prevented and to provide patients with optimal treatment in the presence of this type of complication.

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