Pain Is Significantly Reduced by Cryoablation Therapy in Patients With Lateral Minithoracotomy

Jan Bucerius, MD, Sebastian Metz, MD, Thomas Walther, MD, Nicolas Doll, MD, Volkmar Falk, MD, Anno Diegeler, MD, PhD, Rüdiger Autschbach, MD, PhD, and Friedrich W. Mohr, MD, PhD

Department of Cardiac Surgery, Heartcenter, University of Leipzig, Leipzig, Germany

Background. **In minimally invasive cardiac surgery use of a lateral minithoracotomy is associated with early postoperative rehabilitation but also relatively high pain levels during the first 3 postoperative days. Cryoablation therapy was evaluated prospectively.**

Methods. **From April 1999 until September 1999, 57 patients underwent lateral minithoracotomy for mitral valve operation (n = 18) or minimally invasive direct coronary artery bypass grafting (n = 39). Intraoperatively, patients were randomly assigned to cryoablation or intercostal application of local anesthetic agents. A standardized questionnaire was used for prospective pain assessment on postoperative days 1 to 7.**

Results. **From postoperative day 1 to 7 pain levels declined in all groups. Overall pain levels were significantly lower in the cryo group than in the control group ($p < 0.0001$, GLM). According to diagnoses, pain levels were significantly lower after MIDCABG and cryo versus control; after mitral valve operation they were lower in the cryo group and almost reached significance.**

Conclusions. **Cryoablation is easy to perform and leads to a significant reduction in pain and lower request for additional pain medication after lateral minithoracotomy in minimally invasive cardiac operation.**

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Minimally invasive direct coronary bypass grafting (MIDCABG) or mitral valve operation through a left or right anterolateral minithoracotomy has the advantage of reduced trauma, shorter recovery times, and improved cosmetic results [1, 2]. However, after minimally invasive cardiac surgery (MIS) patients suffer significantly more pain for 2 days when compared with sternotomy. This may counteract the advantages of the less traumatic operation and potentially earlier mobilization [3].

Intercostal application of local anesthetic agents (bupivacaine HCl; Carbostesin; Astra GmbH, Elz, Germany) resulted in only partial reduction of pain. Therefore, cryoablation therapy for postoperative pain reduction has been applied.

For the past 10 years or so there have been various applications of cryotherapy including therapy for liver tumors or cryostripping of varicose veins of the lower limbs or to reduce pain in thoracic surgery [4]. The aim of this study was to prospectively evaluate cryoablation of the intercostal nerves with intercostal catheter application of local anesthetic agents regarding postoperative pain reduction after MIS coronary—or mitral valve—surgery through an anterolateral minithoracotomy.

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Address reprint requests to Dr Bucerius, Department of Cardiac Surgery, Heartcenter, University of Leipzig, Russenstrasse 19, D-04289 Leipzig, Germany; e-mail: bucerj@medizin.uni-leipzig.de.

Material and Methods

From April to September 1999, 57 patients were included in a prospectively controlled study. Thirty-nine patients underwent minimally invasive coronary bypass grafting (MIDCABG). Twenty-one patients were treated with cryoablation of the intercostal nerve (cryo MIDCAB), and 18 received local anesthetic (bupivacaine HCl; Carbostesin, control MIDCAB) for postoperative pain reduction. Mitral valve operation was performed in 18 patients, 9 had cryoablation (cryo mitral), and in the other 9 local anesthetic agents were used (control mitral).

Patients were assigned to one of these therapies by chance intraoperative randomization. The MIDCABG was performed through a left anterolateral minithoracotomy in the fifth intercostal space. Preparation of the left internal mammary artery was performed by lifting of the cranial ribs using different commercially available spreaders.

Minimally invasive mitral valve procedures were performed through a right anterolateral minithoracotomy in the fifth intercostal space. In these patients extracorporal circulation was established via the right femoral vessels using an endoaortic clamp (Port Access, Heartport, Redwood City, CA) or a direct clamp, respectively.

An Erbokryo (ERBE Elektromedizin GmbH, Tübingen, Germany) cryosurgical system was used. The cryoprobe was placed to the perinerval muscular tissue at the fifth intercostal space and N_2O gas at $-80°C$ was applied three times for approximately 2 minutes. No additional pain medication was given intraoperatively.

Intraoperative intercostal application of local anes-

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Table 1. Preoperative Patient Characteristics

	Total	Cryo	Control	*p*
MIDCABG	39	21	18	
Mitral valve operation	18	9	9	
Gender				
Male	63.2%	56.7%	70.4%	
Female	36.8%	43.3%	29.6%	
Age (years)	56.7 ± 12.6	56.25 ± 7	57 ± 15.4	NS
BSA (m^2)	1.88 ± 0.17	1.91 ± 0.14	1.85 ± 0.21	NS
EF (%)	62.7 ± 14.7	57.6 ± 15.5	66.1 ± 13.4	NS

BS = body surface area; Control = catheter application of local anesthetic gents; Cryo = cryoablation therapy; EF = ejection fraction; MIDCABG = minimally invasive direct coronary artery bypass grafting; NS = not significant.

thetic agents (control group) was performed by injecting a single dose of 50 mg bupivacaine HCl (Carbostesin) diluted in 20 ml NaCl into the fifth intercostal space. No further intraoperative pain medication was given as well.

During the postoperative period all patients received additional nonsteroidal antiinflammatory drugs (NSAID; ibuprofen, Imbun) or morphine-like analgetics (piritramid, Dipidolor [Jannsen-Cilag GmbH, Neuss, Germany]; tramadol HCl, Tramal) on demand.

Pain intensity was quantified using the verbal rating scale (VRS) and the visual analog scale (VAS). All patients were interviewed on a daily basis up to the seventh postoperative day using a standard pain questionnaire [3]. Both interviewers were blinded for the applied pain therapy. In addition, patients were asked about postoperative numbness around the incision in the left or right fifth intercostal space. All patient interviews were completed on a daily basis until the seventh postoperative day. A total of 399 questionnaires were analyzed. No patient had had medication for chronic pain preoperatively.

Preoperative demographics are shown in Table 1. A total of 52.6% of the patients were treated with cryoablation for postoperative pain reduction. There were no significant differences between cryo and control groups regarding age, body surface area, left ventricular ejection fraction, and preoperative risk factors. Results are given as mean ± standard deviation. Statistical analysis was performed using a general linear model (GLM) for repeated measures (SPSS statistical package; SPSS, Chicago, IL). Testing for normal distribution pain levels for each postoperative day was analyzed using the Student's *t* test for independent samples.

Results

All 399 questionnaires rendered sufficient information for further evaluation. All patients mentioned that additional postoperative pain medication was sufficient if requested. Furthermore, every patient was reminded that in case of severe pain additional pain medication was available at all times upon request.

Between cryo and control groups there were no significant differences regarding the duration of mechanical ventilation (10.4 ± 9 versus 9.3 ± 7.3 hours; p = NS), requirements for blood transfusion, duration of intensive care, total hospital stay, and the length of chest tube drainage (39 ± 25 versus 34 ± 12 hours; p = NS).

In all groups patients were suffering the most pain during coughing and in-bed mobilization. Pain levels according to the VAS are given in Table 2. In most cases patients were able to get back to preoperative activity levels after removal of the chest tubes. When patients suffered pain it was temporary and described as dull and aching. No differences in pain intensities were observed between all groups when analyzed for patient sex or age.

Pain intensities for postoperative days 2 and 7 according to the verbal rating VRS are shown in Figure 1. Pain levels on postoperative day 2 were relatively higher than on postoperative day 7 in all groups (Fig 1A and 1B, respectively). Before discharge the pain levels decreased in all groups and most patients had no or only mild to moderate pain levels.

With regard to the applied pain therapy, pain intensity was higher in the control groups being more frequent in the moderate or severe category. Pain in the MIDCABG control group on day 2 was more intense compared with the mitral control group, whereas pain in both cryo groups was almost equally low (Fig 1). Pain levels according to VAS are given in Figures 2, 3, and 4. Overall pain

*Table 2. Comparison Between Cryo and Control Groups for Postoperative Day 1 to 7 According to the Visual Analog Scale (*t *Test for Independent Samples)*

	Day						
	1	2	3	4	5	6	7
Mitral							
Cryo	2.41	2.1	2.31	2.18	1.77	1.68	1.1
Control	2.75	2.5	3.38	3.13	3.12	3.62	2.0
p	0.71	0.63	0.23	0.22	0.03[a]	0.04[a]	0.22
MIDCABG							
Cryo	2.0	1.67	1.33	1.33	1.33	1.67	1.33
Control	5.69	4.07	4.85	3.69	2.62	1.69	1.15
p	0.02[a]	0.08	0.01[a]	0.03[a]	0.29	0.98	0.89

[a] $p < 0.05$.

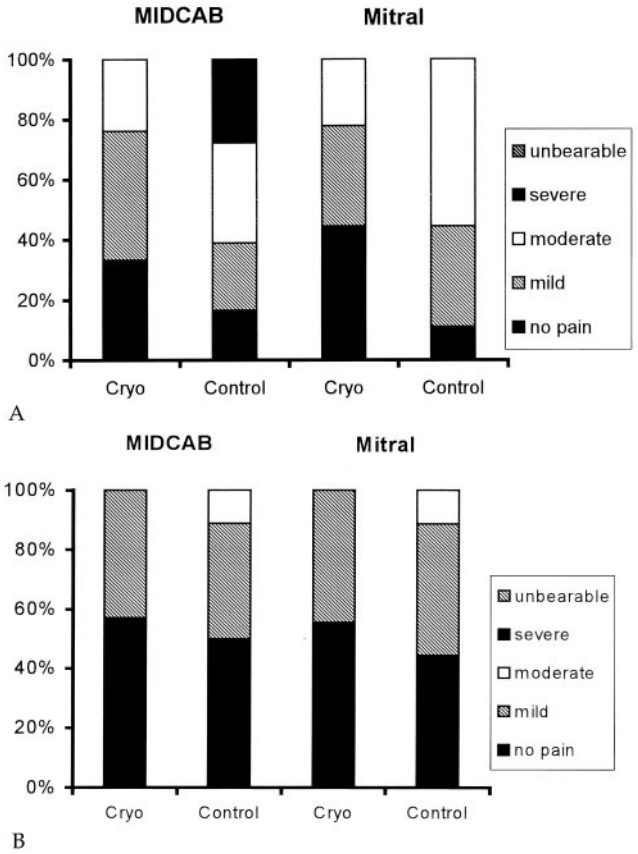


Fig 1. Pain levels according to the verbal rating scale. (A) Postoperative day 2; (B) postoperative day 7. (Control = *catheter application of local anesthetic agents;* Cryo = *cryoablation therapy;* MIDCAB = *bypass grafting;* Mitral = *mitral valve operation).*

in the cryo group decreased from 2.36 (±2.1) down to 1.12 (±0.78) and in the control group from 4.57 (±2.65) down to 1.48 (±2.5). In both groups patients suffered the most pain on the first 3 postoperative days. From the third day onward further improvement was noticed for all patients.

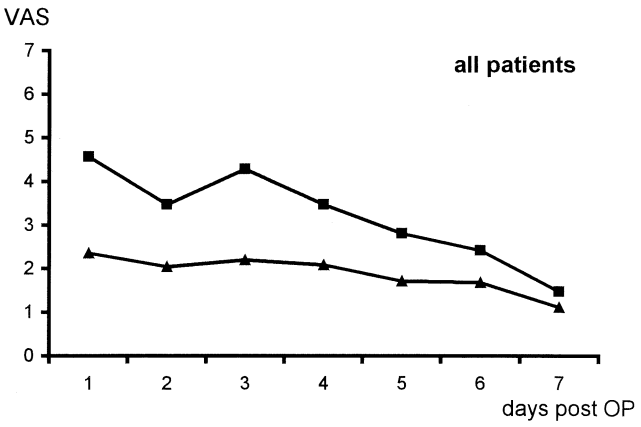
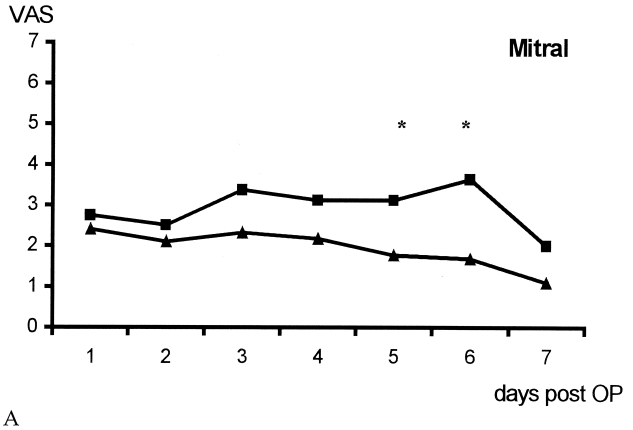


Fig 2. Overall pain levels for cryoablation (▲) versus catheter application (■) for postoperative pain reduction according to the visual analog scale (VAS).



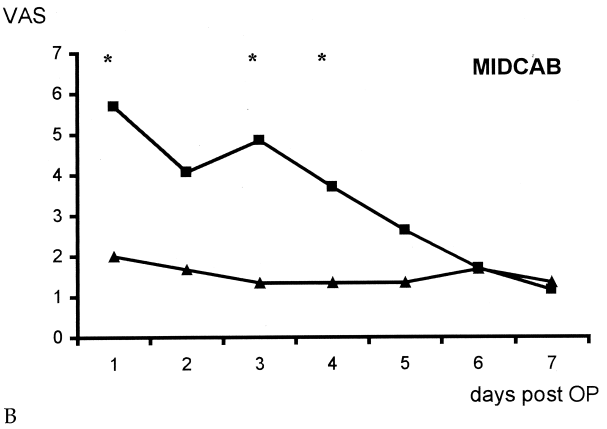


Fig 3. Pain levels for cryoablation (▲) versus catheter application (■) for postoperative pain reduction according to the visual analog scale (VAS). *(A) Mitral valve operation; (B) bypass grafting.* *p < *0.05.*

Overall pain levels for postoperative day 1 to 7 (MIDCABG and mitral) were lower in the cryo group in comparison with the control group ($p < 0.0001$; GLM). There was a significant decline in both groups from postoperative day 1 to 7 ($p < 0.0001$; Fig 2).

In mitral valve surgery overall pain levels decreased from 3.62 (±3.7) to 1.1 (±0.81) as shown in Table 2. Although mitral valve patients suffered less pain after cryo on all days the difference was only close to reaching statistical significance ($p = 0.071$; GLM). In the mitral cryo group a significant decline from postoperative day 1 to 7 was observed ($p = 0.029$; GLM) in contrast to the mitral control group ($p = 0.47$; GLM; Fig 3A). Between mitral cryo and control group the analysis for each postoperative day showed a significant difference on postoperative day 5 and 6 as shown on Table 2.

After MIDCABG overall pain decreased from 5.69 (± 2.39) to 1.15 (± 2.03). Between MIDCABG cryo and control groups a significant difference in pain levels was observed for postoperative day 1 to 7 ($p = 0.03$; GLM). Within MIDCABG cryo there was no significant decline in pain levels from postoperative day 1 to 7 ($p = 0.25$; GLM). However, in the MIDCABG control group pain declined significantly from postoperative day 1 to 7 ($p <$

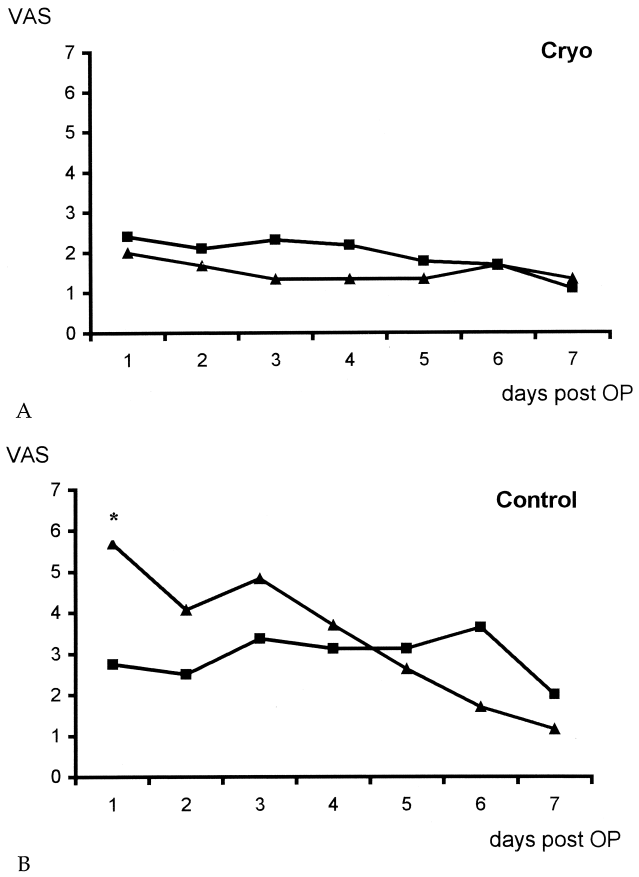


Fig 4. Pain levels for MIDCAB (▲) versus mitral (■) surgery according to the visual analog scale (VAS). *(A) Cryoablation therapy; (B) catheter application of local anesthetic agents.*

0.0001; GLM; Fig 3B). On postoperative days 1, 3, and 4 pain levels differed significantly between MIDCABG cryo and control groups as shown on Table 2.

There was no statistically significant difference between MIDCABG and mitral within the cryo and within the control groups as shown in Figures 4A and 4B (p = 0.49 and 0.51, respectively; GLM). Furthermore, no significant difference was observed between both cryo groups when compared on each postoperative day using the t test (Table 3). In the control groups a statistically significant difference was found on postoperative day 1 between MIDCABG and mitral (p = 0.01; t test).

Request for additional postoperative pain medication was highest on postoperative 1 or 2 for NSAID (Imbun) and opioids (Tramal or Dipidolor). There was a significant decline until discharge in all groups (p = 0.027, p = 0.04, p = 0.048, respectively; GLM). No significant difference was observed between cryo and control groups on postoperative days 1 to 7 (p = 0.235, p = 0.24, p = 0.54, respectively GLM).

Postoperative numbness around the lateral incision after cryoablation therapy was observed by 16.7% of the patients. However, numbness around the incision was transient, no patient mentioned numbness after postoperative day 4.

Comment

Postoperative pain is an important end point to evaluate the impairment of physical and psychological well-being, especially after minimally invasive cardiac procedures [5, 6]. Postoperative assessment of pain is not easy and reliable data are difficult to collect because of the individual pain perception in each patient. With the use of standardized questionnaires and scoring systems these data can be partially quantified [7, 8].

In 1997 Walther and associates [3] examined differences regarding postoperative pain and quality of life and observed relatively higher postoperative pain levels during the first 2 days after lateral minithoracotomy than after the conventional approach. As a result of this study we performed intraoperative injection of local anesthetic agents (bupivacaine HCl, Carbostesin) for postoperative pain reduction. However, postoperative pain remained still high on the postoperative day 2 to 3. There was a consistently high requirement of additional pain medication and delayed mobilization in these patients. Therefore intraoperative cryoablation of the intercostal nerve was introduced for pain reduction therapy. The benefit of this approach was analyzed prospectively in comparison with a randomized control group.

When evaluating the results of this study overall post-

Table 3. Comparison Between MIDCABG and Mitral Groups for Postoperative Day 1 to 7 According to the Visual Analog Scale (t *Test for Independent Samples)*

	Day						
	1	2	3	4	5	6	7
Cryo							
MIDCABG	2.0	1.67	1.33	1.33	1.33	1.67	1.33
Mitral	2.41	2.1	2.31	2.18	1.77	1.68	1.1
p	0.76	0.69	0.38	0.42	0.53	0.98	0.62
Control							
MIDCABG	5.69	4.07	4.85	3.69	2.62	1.69	1.15
Mitral	2.75	2.5	3.38	3.13	3.12	3.62	2.0
p	0.01[a]	0.15	0.17	0.46	0.57	0.11	0.47

[a] $p < 0.05$.

operative pain levels were tolerable for most patients after minimally invasive mitral valve operation or MIDCABG. All patients received sufficient additional pain medication upon request. Furthermore, this study confirms prior findings that daily activities are impaired by postoperative pain and highest pain levels were observed during coughing and mobilization [3]. Pain levels decreased progressively during the first 7 postoperative days, which could have been expected as well. Thus, before discharge on postoperative day 7 no patient suffered severe or unbearable pain according to the VRS.

Postoperative pain levels according to the VAS were highest after MIDCABG procedures on the first 2 postoperative days. On postoperative day 1 there was a significant difference in pain levels between the MIDCABG control and mitral control group. This finding indicates that left internal mammary artery preparation performed while spreading and lifting up the thorax is more traumatic. However, there were no significant differences between the MIDCABG and mitral-cryo groups. This finding underlines the effectiveness of cryoablation therapy indicating an almost complete pain relief. The overall comparison of cryo and control groups regardless of diagnoses revealed significantly lower pain levels after cryoablation therapy. Most of the patients did not suffer any pain even on postoperative day 1.

As mentioned above patients in the MIDCABG control group suffered significantly more pain compared with MIDCABG cryo from postoperative day 1 to 7, indicating the sufficient pain reduction due to cryoablation despite the more traumatic operative approach. Furthermore, daily comparison of pain levels between both groups revealed significant differences for days 1, 3, and 4. Thus cryoablation led to a significant reduction of pain in the early postoperative period. This observation is important as during the first postoperative day patients usually suffer the most pain as was found for the control group and in previous studies as well [3].

In the mitral groups no significant differences between cryo and control were observed from postoperative day 1 to 7. This finding can be explained by the less traumatic technique. To reach the mitral valve less spreading of the intercostal space is required. Thus, although pain levels in the mitral cryo group were lower than in the mitral control group the difference did not reach statistical significance.

With regard to additional postoperative pain medication the overall requirement was low. Because of this, statistical evaluation was performed for cryo and control in total rather than comparing cryo and control with regard to the diagnosis and performed operation. Requirement for NSAID and both opioids was highest on the first 2 postoperative days and declined progressively from postoperative day 1 to 7 in each group. Pain medication both for NSAID and opioids from postoperative day 1 to 7 was lower in the cryo group, although differences did not reach statistical significance. However, when evaluating the reasons for postoperative pain medication we found that in most cases requirement in the control group was related to pain at the surgical incision whereas in the cryo group patients request for additional pain medication was mostly due to the chest tube. In our opinion it is very difficult to evaluate postoperative pain medication because of the various reasons for requirement. Nevertheless we tried to discriminate between pain medication for pain around the surgical incision and that for other reasons; this discrimination was possible by using the standardized questionnaire.

In conclusion, for minimally invasive cardiac procedures through a lateral minithoracotomy, cryoablation therapy is a sufficient and safe method for postoperative pain reduction as compared with intraoperative application of local anesthetic agents. Furthermore, cryoablation leads to a lower requirement of additional pain medication. To prove the benefit of this method especially with regard to long-term follow-up further evaluation will be necessary.

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