Post-Operative Chronic Pain Control in Mediastinal Lymphomas in An Elderly Population: the Role of Physical Activity

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Short title: Sport training in elderly patients with Post-operative pain

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Abstract

Thoracotomy is one of the most painful types of incision a patient can experience. Pain is a very complex pathophysiological entity. Neuronal pathophysiological mechanisms are integrated

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with the immunological response, which amplify inflammation and pain. Prolonged inflammation induces a pathological response of the immune-system and constantly stimulate the nociceptive pathways generating chronic pain. The mechanisms are particularly altered in lymphomas, where pain following chest surgery often becomes chronic and reduces the quality of life.

In this study 51 elderly patients who had undergone a transthoracic biopsy to verify the suspect of mediastinal lymphoma were examined for pain reduction with oral opioids, effect of epidural analgesia and paravertebral block. Subsequently, patients underwent tensed torsion exercises, progressively intensified. After the first few days, patients walked progressively for 20 minutes a day. Once discharged a program of patients started aerobic exercises to increase muscle endurance and to strengthen the extensor muscles of the legs and of the upper limbs.

The systemic administration of opioids is the simplest and most common method of providing analgesia for postoperative pain, but early mobilization, respiratory rehabilitation, and muscle toning exercises are excellent support devices both for physical and psychological recovery.

Keywords: physical activity; elderly population; chronic pain; mediastinal lymphomas

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1. Introduction

Thoracotomy can be one of the most painful types of incision a patient can experience [1]. Pain can inhibit effective coughing, deep breathing and limit early postoperative loosening [2]. As a result, lung ventilation may not be optimal, with an increased risk of lung infections, this is emphasized with advancing age [4]. In addition, inadequate postoperative pain management may contribute to the development of a chronic post-thoractomy pain syndrome [5]. Therefore, the clinicians should maintain an analgesic regimen providing pain relief and consequently the ability to maintain their residual functional capacity through deep breathing [6]. Indeed, an effective elimination of secretions by coughing and early mobilization can lead to faster recovery and to a shorter hospital stay. Pain is a very complex pathophysiological entity, which does not depend exclusively on trauma, but often it has multiple etiologies especially in elderly patients with lymphomas or other neoplasms. Prolonged inflammation induces a pathological response that persists beyond the recovery, constantly stimulating the nociceptive pathways and thus generating chronic pain [7-10]. Neuronal pathophysiological mechanisms are integrated with the immunological response [10-12], the overproduction of cytokines such as IL-6, TNF-α, IL1-β by macrophages and monocytes which amplify inflammation and pain. Instead, both activated B and T lymphocytes have an inhibitory action on pain for the production of IL-10, the cytokine with the highest inhibitory action on the secretion of IL-1β, IL-6 and TNF-α [13-15]. Especially in lymphomas, but also in other neoplasms, the mechanisms involving these cells are altered, helping to not amplify neuropathic pain [16-20]. It is evident that the complexity of the pathogenesis of neuropathic pain does not allow unambiguous solutions in these patients who should be mobilized immediately after surgical procedures [21]. As soon as they are able to, they should undergo tensed torsion exercises which should be progressively intensified. After the first few days, walks should be progressively faster for 20 minutes a day [22-23]. Once discharged, aerobic exercise to increase muscle endurance, and to strengthen the extensor muscles of the legs and of the upper limbs are recommended [24-26]. Early mobilization and small exercises promote respiratory function, contrast the inflammatory mechanisms described above and lower the sensation of pain; another fundamental role, especially in patients with upper caval syndrome, is the support to the lymphatic drainage and to the antithrombotic prophylaxis [27-28]. The systemic administration of opioids is the simplest and most common method of providing analgesia for postoperative pain, but it can be associated with several side effects, such as respiratory depression, sedation, nausea and vomiting. Epidural thoracic analgesia is commonly considered the gold standard to limit the post-operative pain after thoracotomy but in some cases this technique may fail or it may be contraindicated. In fact, epidural analgesia has been found associated with complications like hypotension, epidural hematoma, nerve injury, and shoulder pain at the

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ipsilateral side of the incision [28-29]. The origin of this pain has not been completely elucidated and additional methods of postoperative pain control are considered of enormous interest [30-32].

In our study 51 elderly patients who had undergone a transthoracic biopsy to verify one suspect of mediastinal lymphoma were examined for pain reduction with oral opioids, effect of epidural analgesia and paravertebral block [33-36].

2. Materials and Methods

Our study samples consist of 51 consecutive patients, aged 57 - 84 years who underwent transthoracic biopsy for suspected mediastinal lymphoma, from January 2017 to October 2019, at the Pain Department, AO Dei Colli, Naples, Italy. All clinical procedures were performed in accordance with international guidelines, the standards of human experimentation of the local Ethics Committees and with the Helsinki Declaration of 1975, revised in 1983. At the baseline visit, each patient signed a informed consent for the use of their data in clinical investigation, according with the Italian lows on privacy and underwent a complete physical examination. Their thoracic pain was evaluated with the McGill Pain Questionnaire (MPQ), recording the Numerical Rating Scale (NRS) of average pain: minimum pain, maximum pain and pain during exertion (scale 0-10: 0 = no pain, 10 = worst pain ever). Patients were also tested for HBsAg, anti-HCV, total anti-HBc, and anti-hepatitis B surface antibody (HBs) using specific commercial immunoenzymatic assays as described in previous studies [37-41]. All 51 patients underwent tensed torsion exercises, progressively intensified. After the first few days, patients walked progressively for 20 minutes a day. Once discharged a program of patients started aerobic exercises to increase muscle endurance and to strengthen the extensor muscles of the legs and of the upper limbs.

3. Results

The demographic and clinical data obtained at the enrolment are shown in Table 1 and 2. The 51 patients were predominantly male 34 (67%), with a median age of 68.12 years (range: 57-84). Of those 51, 17 patients underwent to a thoracotomy and 34 patients Video-Assisted Thoracoscopic Surgery (VATS). The intensity of pain after the surgical procedure was very intense (NRS:10) for only one patient, 9 patients had NRS 8, 25 NRS 6, 10 NRS 1, for the remaining 6 the NRS was not detected. The patient with NRS 10 had undergone a VATS and was treated with systemic opioids analgesia during hospitalization. Of the 9 patients with NRS 8, 7 had been treated with systemic

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opioids (2 received VATS and 5 thoracotomy and 2 were treated with PVB both with VATS biopsy). Of the 25 patients with NRS 6, 16 had been treated with systemic opioids of which 8 had undergone VATS and 8 thoracotomy; 5 had been treated with PVB (all had undergone a biopsy with VATS) and 4 with TEA of which 3 with a thoracotomy and 1 with VATS.

4. Discussion and Conclusions

Pain following chest surgery often becomes chronic and reduces the quality of life. Scar pain is a complex entity of multifactorial origin present also in minimally invasive surgery. Early mobilization, respiratory rehabilitation, and muscle toning exercises are excellent support devices both for physical and psychological recovery, since they play an action on the reduction of inflammation, improve the quality of life and give optimism to elderly patient who always lives with particular concern for the onset of a new illness. Epidural thoracic analgesia is considered the best postoperative pain therapy after thoracotomy, but when this technique is contraindicated or fails it should look for other innovative or pioneering solutions.

Appendix

Table.1 Patient treated with systemic opioids analgesy after biopsy.

Age (years)	Sex	Surgery type	Pain relief (NRS)
64	F	THORACHOTOMY	8
80	M	THORACHOTOMY	6
69	M	VATS	6
84	M	VATS	1
74	F	VATS	6
77	F	VATS	8
77	M	VATS	8
58	M	VATS	1
60	M	VATS	8
59	F	VATS	6
61	F	VATS	6
76	M	VATS	1
65	M	VATS	8

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62	M	THORACHOTOMY	6
57	M	VATS	6
59	M	THORACHOTOMY	6
59	M	THORACHOTOMY	6
76	M	VATS	1
71	M	VATS	1
71	M	THORACHOTOMY	6
71	F	THORACHOTOMY	6
70	M	VATS	1
61	M	THORACHOTOMY	6
70	M	VATS	6
72	F	VATS	N.D.
70	F	VATS	6
80	F	VATS	8
70	M	VATS	N.D.
64	F	THORACHOTOMY	8
80	M	THORACHOTOMY	6
69	M	VATS	6
84	M	VATS	1
74	F	VATS	10

Video-Assisted Thoracoscopic Surgery (VATS)

Table 2 Patient treated with PVB or TEA after biopsy.

Age (years)	**Sex**	**Surgery type**	**PVB/TEA**	**Pain relief (NRS) (0-10)**
73	M	THORACHOTOMY	TEA	N.D.
73	M	VATS	PVB	6
64	F	VATS	PVB	8
57	F	VATS	PVB	N.D.
68	F	VATS	PVB	1

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72	M	VATS	PVB	6
62	F	VATS	TEA	1
80	M	VATS	PVB	6
57	M	THORACHOTOMY	TEA	N.D.
60	F	VATS	TEA	6
64	F	VATS	PVB	N.D.
60	F	THORACHOTOMY	PVB	6
67	F	VATS	PVB	1
64	M	THORACHOTOMY	TEA	6
62	M	VATS	PVB	6
61	M	VATS	PVB	8
68	M	THORACHOTOMY	TEA	6
68	F	THORACHOTOMY	TEA	6

Video-Assisted Thoracoscopic Surgery (VATS)

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