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ORIGINAL ARTICLE - THORACIC

Evaluation of arm function and quality of life after trimodality treatment for superior sulcus tumours†

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Abstract

OBJECTIVES: Following trimodality treatment for superior sulcus tumours (SSTs), the 5-year survival rate has significantly improved. Quality of life and potential negative effects of this strategy have become more important. The objective of this study was to investigate the quality of life and the arm and shoulder function after the resection of superior sulcus tumours following neoadjuvant chemoradiation.

METHODS: Patients were selected from a thoracic surgery database. Between January 2002 and December 2010, 72 patients received trimodality treatment of whom 39 were alive at the start of this study in 2010. The following arm function tests were used: nine-hole peg test, range of motion test and action research arm test. Quality of life was assessed using the Disability of the arm and shoulder and SF-36 questionnaires. Analyses of the arm function were conducted comparing the treated side with the untreated side. For quality of life, patients treated on their dominant side were compared with those treated on their non-dominant side.

RESULTS: In total, 19 patients participated in this study (15 men and 4 women). The median age was 59 years (range 39–73), median radiation dose 50 Gy (range 39–66) and median follow-up 40 months (range 4–101). There was no statistically significant difference in arm and shoulder function between the treated and the untreated arm. However, statistically significantly less pain was found if patients were treated on their dominant side.

CONCLUSIONS: After the resection of SSTs following chemoradiotherapy, the arm and shoulder function on the affected side is comparable with the functions at the contralateral side. Patients treated for an SST on their dominant side are less affected in their quality of life regarding pain compared with those treated on their non-dominant side.

Keywords: Superior sulcus tumour • Pancoast tumour • Quality of life • Functional outcome • Arm function

INTRODUCTION

Superior sulcus tumours (SST), also known as Pancoast tumours, are a subgroup of non-small-cell lung carcinomas (NSCLCs) that arise near the pulmonary apex or superior sulcus. They generally invade the chest wall, brachial plexus and, occasionally, the spine or subclavian vessels [1]. After the initial description by Henry Pancoast in 1932, when SSTs were considered to be uniformly fatal, treatment of these tumours has significantly evolved. Neoadjuvant chemoradiation followed by surgery has been the recommended approach for SSTs since 2003 [1–3].

This treatment strategy has resulted in improved survival rates, but the *en bloc* resection of the involved chest wall, brachial plexus and large vessels can significantly influence arm and shoulder function with considerable impact on the quality of life [1, 3]. There is no relevant literature evaluating the impact of SST on the function of the upper extremity and the quality of life. Better insight into the long-term implications of this treatment could be a valuable to aid in preoperative counselling. Additionally, perioperative supportive treatment (i.e. physiotherapy) could possibly be optimized to preserve upper extremity function and improve the quality of life. In this study, the arm and shoulder function, as well as the quality of life, after trimodality treatment for SSTs was investigated.

Our study is based on three hypotheses:

(i) The arm and shoulder function of the treated side will be significantly impaired compared with the untreated side.
(ii) Patients treated on their dominant side will report more disabilities and worse quality of life compared with those treated on the non-dominant side.
(iii) Resection of the T1 nerve root in order to obtain radical resection is associated with significantly worse arm function, more disabilities and worse quality of life compared with patients in whom the T1 nerve root could be spared.

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MATERIALS AND METHODS

Patient selection

Approval was obtained from the Ethics Board of the VU University Medical Center. Data of all patients who underwent trimodality treatment between January 2002 and December 2010 for an SST were extracted from our thoracic surgery database. SSTs are defined as NSCLC located at the superior sulcus with the involvement of structures of the apical chest wall above the second rib [1, 4]. Patients who were alive at the start of this study in December 2010 were identified and approached for inclusion in this study. Patients with the pre-existing impaired function of the upper extremity due to causes not related to trimodality treatment (i.e. cerebrovascular accident, trauma, brain metastasis) were excluded.

Trimodality treatment

Eligibility for trimodality treatment was discussed in a multidisciplinary thoracic oncology meeting for all patients. The standard protocol for trimodality treatment after 2004 was concurrent chemo- and radiotherapy followed by surgery. In the case of squamous histology, chemotherapy consisted of one cycle of cisplatin 80 mg/m^2 (Cisplatine Accord, Accord Healthcare B.V., Rijnsbergen, Netherlands) on day 1 and gemcitabine 1250 mg/m^2 (Gemcitabine, Actavis, Baarn, Netherlands) on days 1 and 8.

In the case of non-squamous histologies, chemotherapy consisted of pemetrexed 500 mg/m^2 (Alimta, Eli Lilly Nederland, Houten, Netherlands) on day 1, and two cycles of cisplatin 80 mg/m^2 on day 1 and etoposide 100 mg/m^2 on days 1–3 for 3 weeks. Involved field radiotherapy (46–60 Gy in fractions of 2 Gy) was administered, starting on day 2 of the second cycle of chemotherapy.

Before 2004, sequential chemotherapy consisted of three cycles of cisplatin 80 mg/m^2 on day 1 and gemcitabine 1250 mg/m^2 on days 1and 8 for 3 weeks, followed by involved field radiotherapy (13 × 3 Gy). However, only two patients in this study were treated with this scheme.

Patients without the progression of disease and without signs of distant metastasis were operated preferably 6 weeks after the completion of induction therapy. Pre- and postoperative physiotherapy did not focus on the arm and shoulder function. At thoracotomy, an upper lobe resection was performed with the *en bloc* resection of the involved chest wall. In addition, the T1 nerve root of the brachial plexus was resected when involved. The bronchial stump was covered by a vascularized intercostal muscle flap. Hilar and mediastinal lymph node dissections were always performed. Posteriorly located tumours were typically approached by a Shaw–Paulson technique, while anteriorly located tumours with the involvement of subclavian vessels were resected through a hemi-clamshell incision [5].

Data collection

From the thoracic surgery database, the following data were extracted: patient age, sex, dominant side, induction therapy regimen, clinical staging (cTNM, 7th edition [6]) before and after induction therapy, operative technique, postoperative pathological staging (ypTNM, 7th edition [6]) and postoperative complications.

Assessment of arm and shoulder function

Arm and shoulder function was assessed and quantified using the measurement of the range of motion test [7], the nine-hole peg test [8, 9] and the action research arm test [10]. The range of motion was assessed during physical examination. Any impairment in the range of motion, measured in degrees, was scored using the cut-off values in Table 1.

The nine-hole peg test was used to assess the swiftness of fine motor function of the hands as described previously [8, 9]. A longer time needed to complete this test (in seconds) implies a reduced arm function. The test is validated for the assessment of hand function in patients who experience neurological motoric impairment after a cerebrovascular event [8, 9]. We regarded this test as applicable to our group of patients, as arm function is also impaired due to damage to nerves innervating the arm and shoulder musculature. Finally, the action research arm test was used to assess the ability to handle objects differing in size, weight and shape and therefore can be considered to be an arm-specific measure of functional impairment. The test evaluates 19 items that can be scored at 0–3 points each (maximum score: 57) [10]. A higher score implies a better arm function. The action research arm test is validated for the assessment of arm function in patients who sustained a stroke and we regarded it applicable to our study population based on the considerations mentioned above [10].

Assessment of quality of life

The quality of life was assessed and scored using the SF-36 questionnaire [11] and the Disability of the arm and shoulder (DASH) questionnaire [12]. The latter is frequently used in functional studies to evaluate the quality of life after limb surgery [13, 14]. The Dutch language version of the SF-36 questionnaire has been validated by Aaronson *et al*. [15] not only for general population surveys, but also for studies in patients with cancer. A higher score (maximum 100) implies a better quality of life.

Statistical analysis

Arm function test results found on the operated side were compared with those found on the untreated side. Regarding the quality of life, we compared those patients treated on their dominant side to those treated on their non-dominant side. A second analysis was performed, comparing both arm function tests and quality of life in patients in whom T1 nerve root was resected to those in whom the T1 nerve root could be spared. All statistical analyses were performed using the statistical software package SPSS, version 17.0 (SPSS Inc., Chicago, IL, USA). For the statistical evaluation of the differences between the arm function on both sides and the quality of life, the Mann–Whitney *U*-test was used. Correlation was analysed using the Pearson correlation test. General characteristics were evaluated with the Mann–Whitney *U*-test in the case of numerical outcome variables and Fisher's exact test in the case of binary

Table 1: Cut-off values range of motion

	0–10% impairment (3 points)	10–30% impairment (2 points)	30–50% impairment (1 point)	>50% impairment (0 points)
Flexion (degrees)	170–153	153–119	119–85	85–0
Extension (degrees)	40–36	36–28	28–20	20–0
Abduction (degrees)	180–162	162–126	126–90	90–0
Adduction (degrees)	40–36	36–28	28–20	20–0
Endorotation (degrees)	60–54	54–42	42–30	30–0
Exorotation (degrees)	95–86	86–67	67–48	48–0

Table 2: General characteristics

	Median (range)	Number of patients
Age at the time of diagnosis (years)	61 (43–71)	
Radiation dose (grey)	50 (36–66)	
Dominant side		
Left		1 (5%)
Right		18 (95%)
Operated on dominant side?		
Yes		15 (79%)
No		4 (21%)
Approach operative technique		
Shaw–Paulson		18 (95%)
Hemi-clamshell		1 (5%)

outcome variables. Missing data were left out of the analysis. Statistical significance was defined as $P < 0.05$.

RESULTS

Patient characteristics

Between January 2002 and December 2010, 72 patients received trimodality treatment for an SST in our hospital. Of this cohort, 39 were alive at the start of this study, of whom 19 patients consented to participate and filled out the SF-36 and DASH questionnaires. Most patients did not want to participate due to the distance of travel between the hospital and their home. Two patients could not participate due to their weak medical condition at the time of this study. The arm and shoulder function was tested in 15 patients. Four patients did not agree to undergo testing of their arm and shoulder function because of the distance between the hospital and their home. Patient characteristics are displayed in Table 2.

Arm function

No significant differences were found when the arm and shoulder function of the treated side was compared with the untreated side. The functional scores, assessed with the range of motion, nine-hole peg and the action research arm tests, are summarized in Table 3.

Table 3: Results from the arm function tests (treated vs untreated side)

	Treated side (mean + SD)	Untreated side (mean + SD)
Range of motion (for scale, see Table 1)	14.73 + 4.83	15.40 + 4.67
Nine-hole peg test (s)	24.92 + 4.92	24.72 + 4.92
Action research arm test	55.20 + 2.54	56.53 + 1.06

Table 4: Quality of life: dominant vs non-dominant side

	Operated on dominant side (*n* = 15; mean + SD)	Operated on non-dominant side (*n* = 4; mean + SD)
DASH	29 + 21	34 + 22
Physical functioning	59 + 18	53 + 33
Social role functioning	77 + 28	75 + 23
Physical role functioning	37 + 44	0 + 0
Emotional role functioning	76 + 43	33 + 47
Mental health	73 + 24	57 + 33
Vitality	56 + 18	49 + 16
Pain	67 + 17	45 + 9[a]
General health perception	59 + 26	50 + 37
Health change	57 + 27	69 + 38

[a]$P = 0.034$ (Mann–Whitney *U*-test).

Quality of life

The results from the quality of life questionnaires (SF-36 and DASH) are displayed in Table 4. Patients operated on their dominant side scored significantly better on the domain pain when compared with those operated on their non-dominant side. For the other domains and the DASH score, no significant differences were found. There were no correlations between the quality of life scores (SF-36 and DASH) and the dose of radiation, age at the time of diagnosis and the operative approach.

Table 5: Arm function test in patients with and without T1 nerve root resection

	T1 nerve root resection (*n* = 9; mean + SD)	T1 nerve root spared (*n* = 6; mean + SD)
Range of motion (for scale, see Table 1)	13.78 + 5.89	16.17 + 2.40
Nine-hole peg test (s)	23.69 + 3.58	26.78 + 6.36
Action research arm test	54.78 + 3.15	55.83 + 1.17

T1 nerve root resection

Subgroup analysis of the arm function tests and quality of life for patients with and without T1 nerve root resection are displayed in Tables 5 and 6. No significant differences could be detected in arm function testing. For quality of life, there was a significant difference in the domain mental health in favour of those patients where the T1 root could be spared.

DISCUSSION

Our study demonstrates that there was no statistically significant difference in arm function between the treated and the untreated side in patients treated with trimodality treatment for SSTs.

In addition, although there was statistically significantly less pain in patients treated on their dominant side, the remaining domains and the overall quality of life were comparable in both groups. In contrast to other studies, no difference could be found between the arm function and quality of life, except for mental health, between patients with T1 nerve root resection and those in whom the T1 nerve root could be spared [16].

To our knowledge, this is the first study investigating the arm and shoulder function and the quality of life in patients treated for SSTs with trimodality treatment. Our study was conducted using validated tests and questionnaires, commonly used to evaluate the arm and shoulder function and the quality of life following upper extremity surgery [12–14].

Several studies have demonstrated a complete resection in 76–93% of patients with 5-year survival rates of over 50% [17–22]. The improved survival nowadays further emphasizes the importance of quality of life in these patients.

Treatment for SSTs could be permanently harmful for the arm and shoulder function as well as the quality of life. The pulmonary apex is in close relationship with many surrounding structures, like the chest wall, brachial plexus, subclavian vessels, stellate ganglion and vertebral column, that can all be damaged by tumour invasion, radiotherapy and surgery.

In the literature, the T1 nerve root is commonly sacrificed, while the C8 nerve root is usually spared. Rusch *et al.* [1] reported that the resection of the T1 nerve root could result in diffuse weakness of the intrinsic muscles of the hand, whereas the resection of the C8 nerve root or lower trunk results in permanent paralysis. To our knowledge, this is the first study investigating the influence of T1 nerve root resection with validated tests and questionnaires on arm function and quality of life.

Table 6: Quality of life in patients with and without T1 nerve root resection

	T1 nerve root resection (*n* = 13; mean + SD)	T1 nerve root spared (*n* = 6; mean + SD)
DASH	33 + 23	24 + 16
Physical functioning	58 + 21	57 + 23
Social role functioning	72 + 29	85 + 18
Physical role functioning	25 + 40	38 + 49
Emotional role functioning	59 + 47	83 + 41
Mental health	63 + 27	85 + 15[a]
Vitality	52 + 18	60 + 16
Pain	62 + 20	64 + 15
General health perception	54 + 30	64 + 25
Health change	58 + 31	67 + 26

[a]$P = 0.046$ (Mann–Whitney *U*-test).

ORIGINAL ARTICLE

Although some other published reports mention that impaired arm and shoulder function can occur, objective measurements of arm and shoulder function have never been published [16, 23, 24]. Shahian *et al.* [23] scaled their functional outcome of shoulder mobility after treatment as excellent, good, fair or poor without exact definitions. Davis *et al.* [16] reported about five patients in whom the C8 and the T1 nerve root were spared during resection. Because three of their patients improved in muscle strength (intrinsic hand muscles), they concluded that C8–T1 should be spared in order to reduce the effects on the intrinsic hand muscles. However, only five patients were described, of whom three improved. In addition, they did not report the hand and arm function in patients in whom the C8–T1 root was not preserved. Our study shows that the arm function as well as the quality of life is comparable in patients with and without T1 resection. Although the T1 nerve root should be preserved when possible, in the case of doubt regarding whether there is tumour invasion, it can be resected without significant consequences for arm function and quality of life.

Our study demonstrates that the function of the treated side is comparable with the untreated side. This might be explained by the fact that most patients were operated on their dominant side. The dominant side is usually better developed. It can also be due to more intensive use after trimodality treatment providing permanent muscle training. In addition, the treatment of an SST may lead to functional improvements since invasion or compression of the brachial plexus by the tumour is resolved by resection. In our experience, arm function, and especially pain, is improved in the phase of induction therapy. Unfortunately, preoperative arm function tests were not conducted in our study population. It would be interesting to compare arm and shoulder function prior to and after trimodality treatment. Such a study is currently conducted in our centre in order to identify the true influence of trimodality treatment on the arm and shoulder function as well as quality of life. Although we expected that the quality of life in patients treated on their dominant side would be significantly worse when compared with those treated on their non-dominant side, this could not be confirmed in this study. We suggest several possible explanations. Patients treated on their dominant side are forced more to train and use their operated arm. Rehabilitation of the function would therefore be quicker, resulting in fewer disabilities and a better quality of life. In addition, the dominant side could have a better developed and trained neurological network due to intensive use in daily life since birth, resulting in a better rehabilitation of the arm and shoulder function. Furthermore, as already mentioned in the previous paragraph, the quality of life of patients with SSTs can also be reduced before trimodality treatment and improve after chemoradiation and resection. For instance, radiotherapy is frequently reported to significantly reduce pain associated with SSTs [25]. Finally, the fact that patients undergo treatment and are potentially cured of cancer can also influence the quality of life in a positive way. Most people take minor disabilities for granted and may not have reported them.

Our study is limited by the small size of the study population of only 19 patients. Due to the limited size, selection bias such as survivorship bias (deceased patients could have had a worse quality of life) or non-response bias (patients with worse quality of life might not be likely to participate in the study) could have existed in this study. Furthermore, sample size calculations were not conducted as this study focused on several parameters and not much is yet known about the arm function and quality of life after trimodality treatment. Therefore, statistical significance should be interpreted with caution. In addition, for the quality of life, we compared patients treated on their dominant side with those treated on their non-dominant side. To investigate the true influence of trimodality therapy, prospective studies are necessary to compare the function of the treated side before and after trimodality treatment and to compare the quality of life before and after trimodality treatment.

In conclusion, the function of the arm on the treated side appears to be comparable with the arm on the untreated side, and the quality of life is the same for patients treated on their dominant and non-dominant sides. Resection of the T1 nerve root appears not to have significant influence on the arm function after surgery. More insight concerning the influence of trimodality treatment is needed in order to determine possible predictors of impaired function and decreased quality of life. We are conducting a prospective study, comparing the arm function and the quality of life before and after resection. We propose, however, the collaboration of several centres treating SSTs in order to achieve a greater number of patients. In addition, a multivariate analysis should be conducted to identify risk factors for impaired function and quality of life that can be influenced to improve patient satisfaction and functional outcome.

Conflict of interest: none declared.

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