Limb-sparing surgery preserves more function than amputation
A SCANDINAVIAN SARCOMA GROUP STUDY OF 118 PATIENTS

We evaluated the long-term functional outcome in 118 patients treated for osteosarcoma or Ewing’s sarcoma in the extremities a minimum of five years after treatment. We also examined if impaired function influenced their quality of life and ability to work.

The function was evaluated according to the Musculoskeletal Tumor Society (MSTS) score and the Toronto Extremity Salvage Score (TESS). Quality of life was assessed by using the Short Form-36 (SF-36).

The mean age at follow-up was 31 years (15 to 57) and the mean follow-up was for 13 years (6 to 22). A total of 67 patients (57%) initially had limb-sparing surgery, but four had a secondary amputation. The median MSTS score was 70% (17% to 100%) and the median TESS was 89% (43% to 100%). The amputees had a significantly lower MSTS score than those with limb-sparing surgery (p < 0.001), but there was no difference for the TESS.

Tumour localisation above knee level resulted in significantly lower MSTS scores and TESS (p = 0.003 and p = 0.02, respectively).

There were no significant differences in quality of life between amputees and those with limb-sparing surgery except in physical functioning. Of the patients 11% (13) did not work or study. In multivariate analysis, amputation, tumour location above the knee and having muscular pain were associated with low physical function.

We conclude that most of the bone tumour survivors managed well after adjustment to their physical limitations. A total of 105 are able to work and have an overall good quality of life.

After the introduction of neo-adjuvant chemotherapy in the 1970s, survival after treatment for a bone sarcoma has improved dramatically, and today the five-year survival for non-metastatic osteosarcoma and Ewing’s sarcoma is approximately 70%. Limb-sparing surgery has been increasingly used with a substantial decrease in the rate of amputation. Limb-sparing surgery can now be performed for up to 95% of patients without compromising the oncological outcome. As survival rates increase, so too does the number of patients living with the consequences of the medical and surgical oncological treatment.

There have been several studies which have described the function and quality of life in bone sarcoma survivors, but many have relatively short follow-up. Most show that limb-sparing surgery is superior to amputation with regards to function, but report no difference in quality of life.

The aim of this study was to evaluate the long-term function of patients treated in Norway and Sweden and to examine if impaired function influenced the quality of life as assessed by the Short Form-36 (SF-36). These patients are young at the time of diagnosis, and most of them have not finished their education or started to work. We also wanted to examine whether their disease and treatment had an influence on their employment status and choice of job.

Patients and Methods
Patients. During 2002 the Scandinavian Sarcoma Group initiated a study to evaluate functional outcome, quality of life and long-term morbidity in patients who were treated for either an osteosarcoma or a Ewing’s sarcoma in an extremity in Sweden and Norway. Inclusion criteria were first, treatment according to one of their osteosarcoma or Ewing protocols; secondly, age ≥ 15 years at follow-up; and finally, an observation period > five years after the end of treatment. Exclusion criteria were inability to communicate in either the Norwegian or Swedish language or mental handicap.

The database revealed eligible patients who...
were contacted by mail or telephone and asked to fill in a questionnaire containing the SF-36 in addition to the hospital anxiety and depression scale, fatigue questionnaires, Impacts of Event Scale and demographic questions.

Patients who returned the completed questionnaire were invited to undergo a clinical examination. Their function was examined using a physical function score (the Musculoskeletal Tumor Society (MSTS) scoring system) and a questionnaire (Toronto Extremity Salvage Score (TESS)).

Surgical procedures. All patients had undergone either limb salvage or amputation. The rate of limb salvage has increased over the years. In the Scandinavian Sarcoma Group II study (1982 to 1989) 73% of patients underwent an amputation whereas in a subsequent study (Scandinavian Sarcoma Group VIII) (1990 to 1997) and in the Italian Sarcoma Group/Scandinavian Sarcoma Group I study (1997 to 2000) 42% and 6% underwent an amputation, respectively. For the Ewing patients the corresponding numbers for extremity tumours were 48% in the Scandinavian Sarcoma Group IV study (1984 to 1990) and 24% in the Scandinavian Sarcoma Group IX study (1990 to 1999).

A total of 165 bone sarcoma survivors were eligible and 155 were contacted and asked to fill in a questionnaire; we were unable to locate ten. There were no ineligible survivors in the database. A total of 133 patients agreed to participate; 130 (84%) returned a complete questionnaire and 110 patients (71%) were assessed clinically. One patient left the outpatient clinic before MSTS or TESS could be performed. Of these 110, three patients were assessed clinically but did not wish to fill in the questionnaire (Fig. 1).

Flow chart showing number of survivors who were eligible and how many agreed to participate in the study (MSTS, Musculoskeletal Tumor Society score; TESS, Toronto Extremity Salvage score).
In this study only patients evaluated according to the MSTS score at the outpatient clinic (109 patients) and/or those who filled in the TESS questionnaire (118 patients) were included.

There were no differences between participants (n = 118) and non-participants (n = 37) in this study regarding age, gender, tumour site, type of treatment or time since diagnosis. The mean age at follow-up was 31 years (15 to 57), and the mean time between diagnosis and evaluation was 13 years (6 to 22) (Table I). A total of 84 survivors (71%) had a follow-up of ten years or more and 37 (31%), more than 15 years. The amputees had a longer follow-up than those with limb salvage (non-parametric Mann-Whitney test, p < 0.001).

Background variables. In addition to demographic variables such as age, gender, civil and employment status we analysed responses to selected questions. Chronic muscle stiffness or pain was evaluated by the single question. ‘Have you during the past year had pain and/or stiffness in muscles and joints lasting three months or longer?’ Whether the disease and treatment had an influence on the choice of career, was derived from the question: ‘Do you think the cancer diagnosis and the treatment have had negative influence on your present employment or education?’

Physical activity was assessed in two levels, first in less strenuous activities such as walking and secondly more strenuous activities that would lead to sweating or breathlessness. At both levels, respondents were asked to define how many hours per week they engaged in these activities. In the final analyses the responses were recoded. ‘No physical activity at any level’ or ‘low level physical activity less than one hour per week’ was defined as ‘physically inactive’. All other responses qualified for ‘physically active’. The questions on physical activity have previously been used in the Health Study of Nord-Trøndelag County (HUNT-2) study,29 and we applied the coding of Thorsen et al.30,31

Functional scoring. The MSTS system is based on six items each for the lower and upper extremities. For the lower extremities the items are: pain, function, emotional accept-
LIMB-SPARING SURGERY PRESERVES MORE FUNCTION THAN AMPUTATION

Limb salvage surgery preserves more function than amputation.

Statistical analysis. The statistical program SPSS 13.01.1 for Windows (SPSS Inc., Chicago, Illinois) was used for all analyses. Means were compared by t-test or analysis of variance with the Games-Howell post hoc correction. Differences between categorical variables were assessed by the chi-squared test. In case of skewed distribution, non-parametric Mann-Whitney tests were used. Logistic regression analyses were used to assess the association between functional caselessness and various demographic and cancer related variables. A p-value < 0.05 was considered to be statistically significant, and all tests were two-tailed.

Results

Of the 118 survivors, 96 (81%) had been treated for osteosarcoma and 22 (19%) for Ewing’s sarcoma. A total of 67 (57%) initially had limb-sparing surgery, but four (3.4%) underwent a secondary amputation, two for infection, one for local recurrence and one for poor function. Two of the 15 survivors (13.3%) treated for sarcoma in the upper extremity underwent an amputation. Reconstruction at limb-salvage mostly involved either autografts/allografts or an endoprosthesis (Table I).

Functional results. The median MSTS score was 70% (17% to 100%). The amputees had a significantly lower MSTS score (non-parametric Mann-Whitney test, p < 0.001) (Fig. 2). The median TESS for all 118 survivors was 89% (43% to 100%). There was no difference between those who underwent an amputation and those with limb-sparing surgery (Mann-Whitney test, p = 0.34).

Tumours above the level of the knee had a significantly lower median MSTS and TESS score (non-parametric Mann-Whitney test p = 0.003 and p = 0.02, respectively) than those below the knee (data not shown). However, for those treated by limb salvage, localisation above the knee did not significantly decrease the median MSTS score or TESS (non-parametric Mann-Whitney test, p = 0.6 and p = 0.32, respectively). For the amputees, amputation above the knee resulted in a significantly lower median MSTS score. The TESS was also lower but not significantly so. Only five patients underwent a below-knee amputation. There was no difference in the median MSTS score and the TESS between those who underwent a disarticulation of the hip and those who underwent an above-knee amputation.

The limb salvage patients treated with allografts showed a higher median TESS (non-parametric Mann-Whitney test p = 0.03) than those with endoprostheses, but there were no difference in MSTS score (Table II).

For the 15 survivors who had tumours in the upper extremity, there was no difference in function whether the tumour had been located in the humerus or forearm (Table II). There were only two amputees, one who underwent disarticulation through the shoulder and one through the elbow.

Quality of life. There was no significant difference in health related quality of life between the amputees and the limb-salvage survivors except in physical functioning, bodily pain and physical component summary scale (Fig. 3). Survivors with a MSTS score < 50% showed significantly lower scores in all physical components of the SF-36.
than those without chronic pain. Cally inactive (chi-squared Fisher's exact test, p = 0.004) with chronic muscular pain or stiffness were more physi-

ence in the level of physical activity between the amputees and the limb-salvage survivors and no dif-

ference between the genders for these parameters. One

half of the patients (59) believed that the cancer had influ-

enced their choice of education or job. These patients

have poorer function that the limb-salvage survivors as

assessed by the MSTS score. This is consistent with other

studies.8,10 Among the amputees, below-knee amputa-
tion results in a significantly better function than above-

knee amputation, and yields a similar function as limb sal-
vage. This finding is in accordance with Pardasaney et al.35

It should be noted, however, that the number of patients

who underwent below-knee amputation in our study was

only five. Below-knee amputation maintains good function

because of limited limb loss and preservation of the knee.

We did not find any statistical differences in the MSTS

score or TESS between those who underwent disarticulation

of the hip and those who underwent an above-knee ampu-
tation. One would expect that hip disarticulation would give

worse function. Only ten patients underwent disarticulation

and those results might be explained by type II errors. To our

knowledge there are no studies comparing the outcome after

disarticulation with that after above-knee amputation.

Discussion

Pre-operative chemotherapy enabling limb salvage without

compromising survival is considered to be a major advance

in the treatment of bone sarcomas of the extremity. Despite

this, a minority of patients still require an amputation. Our

study confirms that limb salvage is superior to amputation

in preserving function.

There are several limitations to our study. Like other

studies performed on survivors of treatment for sarcoma,

we have a relatively small sample and a risk of type II

errors. These trends might turn out to be significant in a

larger sample. In our study, only 118 of 165 (71.5%) eligi-
bile patients are included. Even though we did not find any

statistical differences between the participants and the non-

participants in relation to age, gender, tumour site, type of

treatment or time since diagnosis, there is a risk that the

non-participants might have more problems and worse

function than the participants.

We evaluated the long-term physical function of the

patients treated in Norway and Sweden and found that

most had an acceptable functional outcome. The amputees

have poorer function that the limb-salvage survivors as

assessed by the MSTS score. This is consistent with other

studies.8,13,34,35 Among the amputees, below-knee amputa-
tion results in a significantly better function than above-
knee amputation, and yields a similar function as limb sal-
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worse function. Only ten patients underwent disarticulation

and those results might be explained by type II errors. To our

knowledge there are no studies comparing the outcome after

disarticulation with that after above-knee amputation.

Using TESS we did not find any difference in function

between the patients who underwent amputation and the

limb-salvage survivors. The amputated group had a median

score of 88% and the limb-salvage group of 90%, indicating

that they are coping well which is in agreement with other

studies.8,10 There was a statistical difference in the TESS

comparing above-knee amputation with below-knee ampu-
tation. This is consistent with Ginsberg et al.34 who found a

significant difference in the TESS but not in MSTS scores

between patients undergoing above-knee amputation com-
pared with those undergoing below-knee amputation. In this
LIMB-SPARING SURGERY PRESERVES MORE FUNCTION THAN AMPUTATION

The number of patients undergoing below-knee amputation was also low (4 vs 18).

For the lower extremities we found that those treated with an allograft had a better TESS than those with an endoprosthesis, but there was no difference in MSTS scores between these two groups. There were few survivors in each group, so the results must be looked upon with caution. If an allograft is used, the joint can usually be spared giving better function. Farid et al compared the use of endoprostheses and allografts in the lower limbs and found no statistical difference in the total MSTS scores, but the median hip abductor strength was better in the patients who underwent an allograft prosthetic composite reconstruction. Furthermore, more patients with the alloprosthetic composite could walk without assistance and without a limp.

Assessing functional outcome after surgery for bone tumours is challenging, due to the lack of standardisation of the instruments used. It has been claimed that the MSTS score does not assess the actual physical function. The examiner’s view might influence the results by over- or underestimating the function. Furthermore, this score does not show what the survivor can manage. Davis et al compared the 1987 and 1993 versions of the MSTS, SF-36, scores and TESS. Their conclusion is that the TESS is superior to the other instruments.

The TESS is self-administered and consists of questions about limitations in everyday activities. One reason for not finding any major differences in the TESS between the amputees and those who underwent limb salvage might be that the patients had adjusted well regardless of type of surgery. Hence, it may be argued that the TESS measures the

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**Table II. Musculoskeletal Tumor Society (MSTS) score and Toronto Extremity Salvage score (TESS)**

<table>
<thead>
<tr>
<th></th>
<th>Lower extremity</th>
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<tbody>
<tr>
<td></td>
<td>Type of surgery</td>
<td>Number of patients</td>
<td>Median (range)</td>
<td>p-value*</td>
<td>Number of patients</td>
<td>Median (range)</td>
<td>p-value*</td>
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<tr>
<td>Amputation</td>
<td>48</td>
<td>60 (20 to 90)</td>
<td>&lt; 0.001</td>
<td>53</td>
<td>88 (43 to 100)</td>
<td>NS†</td>
<td></td>
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<tr>
<td>Resection</td>
<td>47</td>
<td>80 (40 to 100)</td>
<td></td>
<td>50</td>
<td>90 (59 to 100)</td>
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<td>Limb-sparing surgery</td>
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<tr>
<td>Above-knee</td>
<td>24</td>
<td>80 (50 to 100)</td>
<td>NS</td>
<td>25</td>
<td>89 (59 to 100)</td>
<td>NS</td>
<td></td>
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<tr>
<td>Below-knee</td>
<td>23</td>
<td>80 (40 to 100)</td>
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<td>25</td>
<td>90 (73 to 100)</td>
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<td>Allografts</td>
<td>18</td>
<td>80 (40 to 100)</td>
<td>NS</td>
<td>18</td>
<td>93 (65 to 100)</td>
<td>0.03</td>
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<td>Endoprosthesis</td>
<td>17</td>
<td>80 (50 to 93)</td>
<td></td>
<td>19</td>
<td>88 (72 to 98)</td>
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<td></td>
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<td>Amputation level</td>
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<tr>
<td>Hip disarticulation</td>
<td>9</td>
<td>47 (27 to 77)</td>
<td></td>
<td>10</td>
<td>89 (62 to 99)</td>
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<tr>
<td>Above-knee</td>
<td>34</td>
<td>60 (20 to 90)</td>
<td>0.007†</td>
<td>38</td>
<td>87 (43 to 100)</td>
<td>NS‡</td>
<td></td>
</tr>
<tr>
<td>Below-knee</td>
<td>5</td>
<td>83 (67 to 90)</td>
<td></td>
<td>5</td>
<td>98 (85 to 98)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper extremity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Tumour localisation</td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Humerus</td>
<td>9</td>
<td>60 (17 to 83)</td>
<td>NS</td>
<td>10</td>
<td>85 (58 to 99)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Forearm</td>
<td>5</td>
<td>70 (30 to 83)</td>
<td></td>
<td>5</td>
<td>90 (78 to 100)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Mann-Whitney test (except amputation level)
† NS, not significant
‡ between disarticulated and above-knee amputation p = 0.42 (ANOVA with Games Howell *post hoc* correction)
§ between above-knee and below-knee amputation p = 0.03

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**Fig. 3**

Short Form-36 (SF-36) dimensions in amputated extremity bone sarcoma survivors and limb sparing survivors (PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health; PCS, physical component summary scale; MCS, mental component summary scale (*non-parametric Mann-Whitney test p < 0.01).
patients’ ability to cope, whereas the MSTS score measures functional impairment. They therefore measure different aspects of function and one is not more relevant than the other.

We also included the SF-36 as an instrument in our study. The amputees had lower physical functioning and physical component summary scores than those undergoing limb salvage, but otherwise there was no difference regarding the health-related quality of life. This finding is consistent with most other studies comparing the health-related quality of life between amputees and patients undergoing limb salvage.6,9-11,16,17,37,38 In contrast, Yonemoto et al39 did not find differences in the physical functioning and physical component summary scores between these two groups, but found that quality of life was better with regard to social functioning scores for the limb salvage group. We did not find this difference. Survivors with an MSTS score of < 50% showed a reduced health-related quality of life compared with the others. This implies that MSTS is a relevant measure of function, and that patients have difficulty coping with poor function, leading to reduction in all aspects of health-related quality of life. One of the most interesting findings of this study was that such poor function (MSTS score < 50%) was almost exclusively found among amputees. Hence, although there appears a limited difference between limb-salvage survivors and amputees as a group, those that fared worst were found among the latter.

In a previous study40 where only Norwegian patients who survived after treatment of an osteosarcoma in an extremity were included, we compared them with an age- and gender-adjusted sample from the general population and other young cancer survivors treated for Hodgkin’s lymphoma or testicular cancer. In that study the sarcoma survivors had significantly lower scores on all the physical dimensions of SF-36 compared with other young cancer survivors and to the general population in Norway.40 Ness et al41 also found that bone sarcoma survivors had physical limitations compared with their siblings.

In this study, we have used the term ‘functional caseness’ for those having an MSTS score < 50% and/or a physical component summary score of < 40. In addition to amputation and tumour localisation above the knee, the only parameter that was significant in multivariate analysis, was chronic muscle pain. Bone tumour survivors may have muscle pain either because of prosthetic problems or altered gait. Hudson et al42 found that survivors of bone tumours were more likely to have cancer-related pain than other survivors of childhood tumours.

Considering employment status, 89% were either working full or part time or still studying and there were no differences between the amputees and limb-salvage survivors. This is consistent with Nagarajan et al’s43 study where 97% were or had been employed and 83% reported having worked the past year. We did not find any difference between the genders in employment status which is in contrast to Nagarajan et al43 who found that men were more likely to be employed regardless of type of surgery. Refaat et al42 reported that men who had undergone an amputation were less likely to be employed than those who had undergone limb salvage. They did not find this association for women. About half of the survivors claimed that the cancer had influenced their choice of career. These patients had lower MSTS scores, TESS and health-related quality of life scores. Poor function might change an individual’s choice of education or job. These survivors often have physical limitations that make them unable to do certain tasks. They might also have long-term sequelae such as impaired hearing due to ototoxicity, heart failure and other complications of chemotherapy that could influence their

### Table III. Short Form 36 (SF-36) dimensions, Toronto Extremity Salvage Score (TESS) and Musculoskeletal Tumor Society (MSTS) score in the patients that think the cancer diagnosis has influenced their choice of education or job

<table>
<thead>
<tr>
<th>Cancer influenced choice of education or job (mean, range)</th>
<th>Yes</th>
<th>No</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>59</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>SF-36 dimensions</td>
<td></td>
<td></td>
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<tr>
<td>Physical functioning</td>
<td>65</td>
<td>76</td>
<td>0.003</td>
</tr>
<tr>
<td>Role physical</td>
<td>66</td>
<td>78</td>
<td>0.06</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>58</td>
<td>78</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>General health</td>
<td>68</td>
<td>79</td>
<td>0.003</td>
</tr>
<tr>
<td>Vitality</td>
<td>56</td>
<td>67</td>
<td>0.004</td>
</tr>
<tr>
<td>Social functioning</td>
<td>81</td>
<td>92</td>
<td>0.01</td>
</tr>
<tr>
<td>Role emotional</td>
<td>75</td>
<td>92</td>
<td>0.001</td>
</tr>
<tr>
<td>Mental health</td>
<td>74</td>
<td>81</td>
<td>0.02</td>
</tr>
<tr>
<td>Physical component summary scale</td>
<td>43</td>
<td>48</td>
<td>0.001</td>
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<tr>
<td>Mental component summary scale</td>
<td>51</td>
<td>55</td>
<td>0.08</td>
</tr>
<tr>
<td>TESS</td>
<td>83</td>
<td>90</td>
<td>0.001</td>
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<tr>
<td>MSTS score</td>
<td>61</td>
<td>75</td>
<td>&lt; 0.001</td>
</tr>
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</table>

* Mann-Whitney test
choice of career. However, these factors have not been considered in this study. The lower health-related quality of life scores among the patients who claimed the cancer had influenced their choice of career might also reflect a pessimistic attitude towards life. However, in the study of Norwegian survivors, there was no difference in the mental dimensions of SF-36 or in the level of anxiety or depression compared with the general population. Since most survivors were still in school at the time of diagnosis, not many can have changed their work due to the cancer or treatment.

A total of 84% of the survivors were considered to be physically active. Those with lower physical function were as active as those with better function. One reason might be that they exercise more to compensate for their limited function. In a study of survivors of testicular cancer, 86% were considered physically active compared with 82% of the general population. Hence, despite the often major physical limitations of bone sarcoma survivors they lead a physically-active life comparable with both the general population and survivors of other cancer types.

We conclude that most of our bone sarcoma survivors manage well. They are able to work and have an overall good quality of life having adjusted to their physical limitations. Although the amputees have poorer function than those who have undergone limb salvage, most have coped well and their health-related quality of life is similar. This is important information to tell the few patients in whom an amputation is necessary. A small group of amputees had very poor function which also affected their health-related quality of life. It is important to help these patients to improve their overall function and well-being.
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References