Review



# MUTARS Prosthesis in Patients with Bone Cancer of Lower Limb: A Narrative Review of Functional Outcomes

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Keywords: MUTARS; bone cancer; functional outcomes; lower limb

*Review*

# MUTARS Prosthesis in Patients with Bone Cancer of Lower Limb: A Narrative Review of Functional Outcomes

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**Abstract:** Limb-salvage surgery is the first choice for treatment of primary or metastatic bone tumors when possible to perform. Rehabilitation plays a major role after surgery, with the aim of improving function and maintaining the highest possible quality of life. Megaprostheses are currently the most frequent type of limb reconstruction used to treat the bone defect after tumor resection and The Modular Universal Tumor And Revision System (MUTARS®)is currently among the most used tumor and revision systems. Several studies have evaluated the causes and rate of failure of this system, but only few studies investigated the rehabilitative outcomes in terms of function and quality of daily life. The aim of this narrative review is to explore the correlations between functional outcomes and quality of life after implant of MUTARS® prostheses surgery in patients with bone tumor of the lower extremities. A comprehensive search was conducted on PubMed and Scopus using the following MESH terms: "MUTARS", "Megaprosthesis", "bone", "tumors", "metastasis", "lower limb", "rehabilitation", "outcome", "quality of life", and 12 studies were included. The most frequent oncological pathology was found to be primitive bone tumors treated with modular prosthesis. Outcome measures used were Henderson et al classification, HHS, MSTS, VAS, ROM,LSR, KPS and quality of life questionnaire. Reconstruction of the lower limbs with the MUTARS® system seemed to be a valid treatment option after bone tumor resection. Rehabilitation after MUTARS® surgery is very relevant, but currently, functional and rehabilitative outcomes are inadequately represented in the literature. Therefore, further studies are needed to define best rehabilitation protocols in clinical practice after oncological orthopedic surgery.

**Keywords:** MUTARS; bone cancer; functional outcomes; lower limb

## 1. Introduction

Primary bone tumors account less than 1% of all cancers while bone metastasis, especially in adults, are much more common. Over the past half century there have been enormous advances in the treatment of bone tumors as a result of advances in diagnosis, therapies and prosthetic design for reconstruction of musculoskeletal defects. Despite the advances in therapies and surgical techniques, long-term functional outcomes have been little studied. Therefore, it is increasingly important to investigate this domain to ensure patients a good quality of life beyond survival.

The three most common primary bone cancers are Osteosarcoma, Ewing sarcoma, and Chondrosarcoma, with different age and site distribution: Osteosarcoma occurs most often in children and young adults, with a peak incidence at ages 10 to 14 years and occurs most commonly around the knee; Ewing sarcoma is most common in teenagers and occurs most commonly in long bones; Chondrosarcoma typically occurs in patients 40 years and older and it usually arise in the

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pelvis or long bones [14]. Considering the site, the most common in malignant bone tumors of lower limbs is distal femur and proximal tibia [13]

Whenever is possible,in patients with primary or metastatic bone tumors limb-sparing surgery is performed. The Modular Universal Tumor And Revision System (MUTARS®)is currently among the most used tumor and revision systems. Megaprosthesis are modular endoprostheses consisting of several different components in promptly available sets, which can be assembled in different combinations to fit the specific skeletal defect allowing limb sparing. It offers the ability to vary the lengths and angles, thus allowing intraoperative adaption to the individual patient's defect [15,16]. Is worth noting that many complications occur after prostheses replacement as tumor surgery is a very traumatic surgery including greater bone and soft tissue resection, blood loss, long time operation with larger exposure range which combined with frequent radio and chemotherapy results in higher rate of post-operative infections, higher risk of loosening and peri-prosthetic fractures. These complications also affect the rehabilitation and have also a potential risk of secondary revision or amputation.

The aim of this narrative review is to describe the short- and long-term functional and rehabilitative outcomes of patients affected by primary or metastatic bone tumor in the lower limb surgically treated with MUTARS® prostheses.

## 2. Methods

A comprehensive search was conducted on Pubmed and Scopus using following MESH terms: “MUTARS”, “Megaprosthesis”, “bone”, “tumors”, “metastasis”, “lower limb”, “rehabilitation”, “outcome”, “quality of life”, in human, in oncological disease without other limits.

A number of 24 articles were assessed for eligibility. After removal of studies considered not relevant -not concern oncological patients or not cited outcome measures of interest- we selected 12 papers by title and abstract, and analyzed them.

Data extracted from the selected studies were: type of study (retrospective or prospective), patients characteristics (number, sex, mean age), type of bone tumors of the lower limb (histological characteristics and distribution between primary and metastatic lesions), the model of prosthesis used for surgical replacement, the outcome measures, timing of follow-up, and the results. The main results are summarized in Table 1.

## 3. Results

The analysis of the selected papers about functional outcomes of patients affected by lower limb primary and/or metastatic bone tumors treated with MUTARS® is summarized in Table 1.

**Table 1.** Description of the included studies.

| Paper | Type of Study | Patients | Bone Tumor Lower Extremity | Model of Prostesis | Outcome Measures | Timing | Results |
|---|---|---|---|---|---|---|---|
| Pala et al. (2021) | Retrospective, multicentric | n: 187<br>M/F: 100/87<br>Mean age (range) 53 (4-89) years | n. 107 malignant bone tumors or soft tissue tumors with bone involvement<br>n. 52 metastatic<br>n. 13 Lymphomas / Myelomas | MUTARS Upper/Lower limbs: 72/115<br><br>Regarding Lower limbs: n.56 cemented<br>n. 59 non cemented | Oncological outcomes<br>n. 143 surgical complications (Henderson et al.)<br><br>n. 139 MSTS score | 2000- 2019<br>Mean oncologic follow-up 3.4 years (range: 1 month–16 years) | MSTS score after surgery:<br>average score 25.1 (9-30)<br>n. 115 (excellent)<br>n. 20 (good)<br>n. 4 (fair)<br>n.0 (poor) |

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| | | | n. 8 Giant cell tumors<br>n. 7 non-oncologic | n.65 silver-coated | | | |
| Bus et al. (2015) | Retrospective | n. 101<br>M/F: 55/46<br>Mean age (range) 36 (13-82) years | n. 56 Osteosarcoma<br>n. 10 Leiomyosarcoma<br>n.9 Chondrosarcoma<br>n. 9 Giant cell tumors<br>n.7 Pleomorphic undifferentiated sarcoma<br>n.5 Ewing sarcoma<br>n.2 Low-grade osteosarcoma<br>n. 2 Sarcoma not otherwise specified<br>n. 1 Synovial sarcoma<br>n.1 Diffuse-type giant cell tumor | MUTARS Knee<br>Cemented/Non cemented: 23/78<br>Hydroxyapatite-coated: 42 | Oncological outcomes<br>n. 63 surgical complications (Henderson et al.) | 1995 -2010<br>Median follow up 8.9 years (range: 8.0-9.7) | Absence of rehabilitation outcomes |
| Kamiński et al. (2017) | Prospective, cohort study | n. 34<br>M/F: 12/44<br>Mean age (range) 72 (45-85) years | n. 13 metastasis<br>n. 21 cases: non oncological prothesis revision | MUTARS Hip<br>Cemented: 34 | HHS<br>M-HHS<br>VAS | Dec. 2008 to Jan 2016<br>Follow up on the first post-operative day and then at 3, 6 and 12 months | Absence of statistically significant differences between groups in HHS, m-HHS and VAS after surgery, although similar improvements in both groups |
| Gosheger et al. (2006) | Retrospective | n. 250<br>M/F: 135/115<br>Mean age (range) 30.7 (7.4-80 ) years | n. 139 Osteosarcoma<br>n. 43 Chondrosarcoma<br>n. 36 Ewing sarcoma | MUTARS Upper/Lower limbs: 51/199<br>Regarding Lower limbs: | MSTS score | 1992-2003<br>Mean follow up 45 months (range: 3-140 months) | Average MSTS score (lower limb): 25, after proximal tibia replacement (range 13-30)<br>24, after distal femoral |

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| | | | n. 15 Pleomorphic sarcoma<br>n.6 Parosteal osteosarcoma<br>n.3 Leiomyosarcoma<br>n.4 Soft tissue sarcoma with bone involvement<br>n.4 Giant cell tumor | n. 58 cemented<br>n. 141 non cemented<br><br>Since 1997 all HA-coated. All cemented prosthesis containing gentamicin. | | | replacement (range 8-30)<br>21, after proximal femoral (range 14-29)<br>20, after total femoral replacements (range 13-27)<br><br>Average MSTS score (upper limb):<br>23, after distal humerus replacement (range 18-27)<br>21, after humerus replacements (range 1-25)<br>19 after total humerus replacements (range 18-20) |
| Pitera et al. (2017) | Retrospective<br><br>Abstract | n. 42<br>M/F: 19/23<br>Mean age 63 ± 11 years | n. 42 proximal femur metastasis | n. 30 GMRS<br>n. 12 MUTARS Hip<br><br>Cemented/ Non cemented: 36/6 | VAS<br>HHS<br>MSTS score | 2012-2015<br>Follow up at 6 weeks after the surgery | n. 39 patients at 6 weeks after the surgery:<br>VAS 3.8 (mean)<br>HHS 75 (mean)<br>MSTS 20 (mean)<br><br>n. 37 (95%) walk efficiently, with crutches or with physical assistance of others |
| Hardes et al. (2018) | Retrospective | n. 98<br>Median age (range) 18 (10–78) years | n. 63 Osteosarcoma<br>n. 16 Ewing sarcoma<br>n. 6 Pleomorphic sarcoma<br>n.6 Giant cell tumour<br>n. 5 Chondrosarcoma<br>n. 1 | MUTARS Knee<br>n. 9 tibia component cemented and hybrid-fixated femur component (cementless stem with cemented shield) | Oncological outcomes<br>Surgical complications (Henderson et al.)<br><br>Knee extension in patients after surgery:<br>n. 51 no deficit<br>n. 11 5°-10° deficit | 1996-2014<br>Mean oncological follow up 45 months (range: 3-140 months) | Absence of rehabilitation outcomes.<br><br>There were no statistically significant associations between an active extension deficit and patella alta. By contrast, patella baja was associated with a noticeable |

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| | | | Leiomyosarcoma n. 1<br>Parosteal osteosarcoma | Silver-coated: 56 | n. 6 > 10° deficit<br><br>Knee flexion in patients after surgery:<br>n. 55 ≥90°<br>n. 9 89°-80°<br>n. 4 40°–70° | | reduction in the number of patients with flexion > 90° |
| Hardes et al. (2013) | Retrospective | n. 59<br>M/F: 36/23<br>Mean age (range): 33 (11 - 74) years | n. 34 Osteosarcoma<br>n. 7 Chondrosarcoma<br>n. 7 Synovial sarcoma<br>n. 7 Pleomorphic sarcoma<br>n. 3 Leiomyosarcoma<br>n. 1 Giant cell tumour of the patella | MUTARS<br>Knee (distal femour, prossimal tibia)<br>n. 14 femur component cemented<br><br>Silver-coated: 33 | Oncological outcomes<br>Surgical complications (classified in major and minor)<br><br>n. 46 MSTS score<br>n. 21 OKS<br>n. 38 ROM of the knee | 1992-2011<br>Mean follow-up 62 month (12 to 211) | Mean MSTS score (range): 22 (10 to 29)<br>Mean OKS (range): 32 (10 to 48)<br>Mean range of flexion (range): 72° (10° to 100°).<br>A total of 25 of these had flexion of ≥ 90°, and only one had gross limitation of movement with flexion of 20° after peri-prosthetic infection and revision<br><br>An orthosis and/or a walking aid were used by 12 patients |
| Guzik (2016) | Retrospective | n. 64.<br>M/F: 38/26<br>Mean age in F: 66 years<br>Mean age in M: 69 years<br>64%of patients had pathological fractures and were unable to walk | n.64 metastatic lytic tumours | n. 36 MUTARS Hip (prossimal femour)<br>n. 28 GMRS<br><br>Cemented/ Non cemented: 19/45 | MSTS<br>VAS<br>HHS<br>KPS | 2010-2014<br>Mean follow up (range): 1.8 (3.6 to 1.2) years | After 6 weeks after surgery:<br>mean MSTS: 20 (18-21)<br>mean VAS: 3.8 (2-5)<br>mean HHS: 75 (71-81)<br>mean KPS: 64 (50-80)<br><br>After 12 weeks after surgery:<br>mean MSTS: 21 (18-22)<br>mean VAS: 3.4 (2-5)<br>mean HHS: 81 (71-86) |

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| | | | | | | | mean KPS: 65 (50-80)<br>Walking:<br>n. 15 patients ambulate efficiently without crutches. n. 39 patients use one crutch or a walking cane when walking over longer distances<br>n. 10 patients walk with two crutches.<br>Muscle strength of the operated limb: lower in all patients.<br>Use of stairs:<br>n. 37 patients with alternating gait<br>n. 27 patients by leading with the healthy limb and following with the affected limb |
| Bernthal et al. (2015) | Observational case-control study | n. 24 oncological group (case)<br>Mean age ( range) : 37 (18.3–63.6) years<br><br>VS<br><br>n. 8 heatlhy adults (control) | Primary lower extremity bone sarcoma | Howmedica, Techmedica, or Stryker (Kalamazoo, MI, USA) Hip-Knee<br><br>All cemented stems | MSTS score<br>$0_2$ consumption<br>Gait speed<br>Knee flexion and extension strength deficit<br>Strides per day | Mean (range) follow up in the gait laboratory 13.2 (2.5–28.2 ) years after surgery | Mean MSTS score 26 (18-29)<br><br>No significant differences between groups in $O_2$consuption test, in walking speed and number of strides per day<br><br>Proximal tibia replacement group had lower strenght in flexion/extension vs other surgery group and vs control group |
| Pellegrino et al. (2020) | Observational case-control study | n. 26 oncological group (case)<br>M/F: 13/13 | n. 12 Osteosarcoma<br>n. 5 Chondrosarcoma | Oncological group:<br>n.10 GMRS<br>n. 9 LINK®<br>n. 7 MUTARS | Gait analysis (basography, knee ROM, electromyographic activity of some | Oncological group: 2006-2016. (minimum follow-up of 12 months) | <u>Gait analysis:</u><br>Mean speed (m/s ±SD): oncological/osteoarthritis: |

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| | | Mean age± SD ( range): 40.9 ± 18.9 years (range: 15–75)<br><br>VS<br><br>n. 21 Osteoarthritis group (control)<br>M/F : 8/13<br>Mean age± SD (range): 68.0 ± 4.7 years (range: 56–74) | n. 4 Giant cell tumor<br>n. 2 Undifferentiated sarcomas<br>n. 2 Leiomyosarcomas<br>n. 1 Primitive bone lymphoma | VS<br><br>Osteoarthritis group: TKA with a posterior stabilized, ultra-congruent or cruciate retaining implant | group of muscles during the gait cycle)<br>ROM of the knee MSTS score (only oncological group) SF-36 | Osteoarthritis group: 2010–2014 (minimum follow-up of 12 months) | 0.83±0.22/0.76±0.21<br>Cadence(stride/min±SD): oncological/osteoarthritis: 47.8±5.4/45.3±6.6<br>No statistically significant differences were detected betweendifferent surgical approaches in the oncological group.<br><u>ROM of the knee:</u><br>Statically significant difference between the healthy limb and the operated one in both groups. However, no significant difference was registered between the limb with megaprosthesisand the limb with a standard implant.<br><u>Mean MSTS score</u> (% ±SD): 79.2±3.9<br><u>SF-36 (subscale):</u><br>The mean value was higher in oncological group in Bodily pain, Vitality, Social functioning and Mental Health.<br>The mean value was higher in osteoarthritis group in General Health. |
| Lopresti et al. (2015) | Observational<br><br>Abstract | n. 28<br>Mean age ± SD: nr | Primary bone tumors | Knee mega-prosthesis | MSTS score | March-May 2013 | n. 24 correct rehabilitation path after surgery |

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| | | | | | | | Median MSTS score (range): 29 (19-33)<br><br>Significant higher scores in physiotherapy patients |
| Ferrara et al. (2019) | Observational | n. 21<br>M/F: 7/14<br>Mean age ±SD: 61.76 ±14.68 | n. 15 metastatic bone tumor<br>n. 6 Osteosarcoma | MUTARS<br>71,4% proximal femour<br>23.8% distal femour<br>4.8% both | ROM<br>VAS<br>SPPB<br>ECOG<br>KPS<br>MSTS score<br>TESS<br>Stabilometry | February 2017-December 2018<br>Follow-up at one week, one month, three months, six months, one year | Significant improvement:<br>VAS at T1<br>hip ROM, MSTS and TESS at T2<br>SPPB at T3<br>No significant results in stabilometry. |

MUTARS: Modular Universal Tumor And Revision System; GMRS: Global Modular Replacement System; TKA: Total Knee Arthroplasty; MSTS: Modular Universal Tumor And Revision System; HHS: Harris Hip Score; M-HHS: Modified-HHS; VAS: Visual Analogue Scale; OKS: Oxford Knee Score; KPS: Karnofsky Performance Scale; ECOG: Eastern Cooperative Oncology Group; TESS: Toronto Extremity Salvage Score; SPPB: Short Physical Performance Battery; SF-36: Short Form Health Survey – 36.

In our review we included 10 full-text articles [1–4,6–10,12] and 2 papers [5,11] evaluated by title and abstract. The studies we selected were: eight retrospectives [1,2,4–8] and five prospective [3,9–12].

The retrospective analysis of the studies selected covers a period between 1992 and 2019. A total number of 963 patients are included, everyone surgically with treated with modular prostheses of lower limbs. The sample size of the studies appears variable, ranging from a minimum of 21[12] to a maximum of 250 subjects [4].

The demographic characteristics of the sample ranges from 4 years to 89 years, so the review covers both pediatric and adult age; mean age of the studies population is 42,1 years old, excluded one article [11] where no data are available. Females are more represented than males in the considered papers, contrary to major epidemiological data. The types of bone tumors included in the studies are disparate, both in histological terms and primary or secondary nature: four papers [2,4,9,11] analyze only primary tumors, two articles study only metastatic lesions [5,8], while most studies collect data regarding both primary and secondary bone lesions [1,3,12]and the remaining articles don't report these informations [6,7,10]. Histological tumors reported are: metastatic bone tumors, osteosarcoma, leiomyosarcoma, chondrosarcoma, giant cell tumors, lymphomas and other primary bone tumors. The most frequent tumor found is Osteosarcoma, in accordance with current epidemiology.

Regarding the site of MUTARS® implant, authors report prostheses replacement of the knee region [2,6,7,10,11], of the hip region [3,5,8], while the remaining articles consider multiple sites of the lower limbs affected by bone tumor [1,4,9,12]. The available evidence in literature, accord to which distal femur and proximal tibia are the most common site of bone tumors in lower limbs [13]. The modular endoprostheses reported in the article are diverse and not always described: 273 cemented, 45 uncemented, 154 silver coated, 42 hydroxyapatite (HA) coated. Furthermore some papers [5,8,10] report also the use of other types of mega-prostheses implants (Global Modular Replacement System®, the Megasystem C®) without comparisons between them in terms of functional outcome.

The outcome measure used are heterogeneous from multiple points of view, showing considerable variability. There are surgical outcomes as Henderson et al classification in three studied

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[1,2,6]; oncological outcomes as No Evidence of Disease (NED), Died With Disease (DWD) and Alive With Disease (DWD) used in four papers [1,2,6,7]. With regard to the aim of this research, the rehabilitation outcomes are so summarized: functional measures as Harris Hip Scale (HHS) in three studies [3,5,8], Harris Hip Scale Modified (m-HHS) in one study [3], Oxford Knee Score (OKS) in one article [7]; objective measures as gait analysis in two studies [10,12], stabilometry and Short Physical Performance Battery (SPPB) both in one study [12]; Visual Analogue Scale (VAS) for the subjective pain in four studies [3,5,8,12]; the range of motion (ROM) of the considered joint in four studies [6,7,10,12]; SF-36 questionnaire for quality of life in one study [10]. Some studies use functional measures specifically for this type of patients: Musculo-Skeletal Tumor Society score (MSTS) in 6 papers [1,4,5,7–12], Karnofsky Performance Scale (KPS) in two studies [8,12], Enneking score in one study [4], Toronto Extremity Salvage Score (TESS) and Eastern Cooperative Oncology Group (ECOG) both in the same study [12].

## 4. Discussion

The results of the included studies are mainly focused on the orthopedic goals, to improve the surgical techniques or to reduce the complications, while the rehabilitative aspects are very poorly represented. Certainly, rehabilitation cannot be separated from the evaluation of surgical, oncological and functional outcomes in orthopedics. Comparison of all the studies is laborious because of all the differences in age,timeframe of follow-up,and individuality

*Functional Outcomes*

The most cited functional measures is MSTS score [1,4,5,7–12]. It is a well-accepted psychometric properties scoring system, although this is not validated in Italy. In all of the studies MSTS score results were good to excellent in the populations who implanted a lower limb megaprosthesis. Particularly in Lopresti et al. paper, MSTS score showed statistically significant higher scores in patients that followed a physiotherapy program after surgery. In Hardes J et al study [7] they considered not only the MSTS score but also the OKS. They observed that although the achievement of good functional results after extra-articular resection, the rates of complications and subsequent amputation were higher than in patients treated with intra articular resection. They also reported that despite the good functional results, several patients needed support when walking and had problems with kneeling, limping and descending stairs.

In Pellegrino et al. study, after the rehabilitation process of a limb-sparing surgery, a good percentage of patients reached a medium-high functionaloutcome and degree of satisfaction, as demonstrated by MSTS results.

The reduction of pain is evaluated with the Visual Analogical Scale in four studies [3,5,8,12].All the results showed a low pain after the implantand at the same time a good physical performance. Guzik et al. demonstrated an accordance between the improvement of the function (evaluated by KPS and MSTS score) and pain.

Such good outcomes were also supported by SF-36 scores. Subjective functional activity of patients who underwent megaprosthesis implant was assessed through the MSTS score: the mean value was 79.2 ± 3.9%. The category that obtained better results was ‘stability’, while the score was heavily influenced by poor results in ‘strength’ and ‘emotional acceptance’. A collateral information about the quality of life is reported in Hardes et al. study. They report the employability after intervention of their sample: of the evaluable 21 patients, 52% (n = 11) worked fulltime and only one was not able to work at all.

In three articles [3,5,8] HHS is assessed and in article [3] is also evaluated the modified-HHS. The HHS is a reliable investigation as to the domains of pain, function, absence of deformity, is associated the physical examination with the range of motions.

In Kamiński et al. patients with tumor metastasis and patients underwent revision surgery due to implant loosening showed statistically significant improvements in pain and HHS scores at follow-up at one year after the procedure.

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All parameters assessed except for prolonged comfortable sitting, putting on shoes and socks, and the ability to use public transport. Everyday self-care required more focus on pain reduction (confirmed also in the VAS scale) and the ability to walk, including climbing stairs, in those after revision arthroplasty, as well as the oncological patients with maintaining and improving comfort of walking. It should be remembered that expectations of patients undergoing another implant revision surgery differ from those of oncological patients or patients after primary arthroplasty.

Also, patients after revision arthroplasty needed for longer rehabilitation due to the need of longer hospitalizationfollowing the procedure. This is explained because of multiple surgical procedures of the musculo-skeletal system conducted during surgerythat affected the baselinefunction of the patients, who thus required longer rehabilitation.

Regarding gait alterations after the surgery, in one article [8] 15 out of 64 patients ambulated efficiently withoutcrutches, 39 patients used one crutch or a walking canewhen walking over longer distances and 10 patients walked with two crutches; muscle strength of the operated limb was lower in all patients; a positive Trendelenburg's sign wasobserved, indicating impaired gluteus function; thepatients were able to use stairs with alternating gait(37 patients) or by leading with the healthy limb andfollowing with the affected limb (27 patients); therewere no knee contractures which would make itdifficult or impossible for the patients to get up from a chair. Gait analysis is investigated in Pellegrino et al. study. They compared gait alterations between patients who had megaprosthetic replacement for tumors around the knee and patients who had total knee arthroplasty (TKA) for osteoarthritis (AO). The results showed that standard TKA and mega-prosthetic implants led to partially similar gait alterations. All patients walked slower than healthy people and cancer group had slow gait velocity because of less strength due to extensive muscle resections and bone sacrifice. In the OA group the limbs tended to adapt with similar stance values by sacrificing speed and increasing the double stance phase, while in the cancer group the stance difference is balanced by the healthy limb so as to maintain a relatively higher velocity. The results showed that gait pattern abnormalities do not affect patients with a megaprosthetic replacement more significantly than patients undergoing TKA. In one article [9] is reported that, at a mean of 13.2 years from the endoprosthetic reconstruction, patients with proximal/distal femoral replacements and proximal tibia replacements, all walked efficiently. In particular patients with proximal tibia replacements had more muscle weakness about the knee, but all groups remained similarly active at home and in the community.

ROM is evaluated in four articles [6,7,10,12]. Pellegrino et al. investigated ROM of the knee in patients withmegaprosthetic replacement for a tumor comparing them with patients with total knee arthroplasty due to osteoarthritis, with no significant difference between the two implants. Ferrara et al investigated the hip and the knee flexion range of movement in a population with MUTARS® reconstructions after proximal or distal lower limb tumor resection. The results showed a significant improvement of hip flexion ROM at the second evaluation at three months, after rehabilitation. There was an increase of the quadriceps muscle strength between T1 and T2, close to the significance (p-value 0.08). The improvement of ROM and muscle strength was progressive, like the self-sufficiency and psychophysical conditions evaluated by SPPB, MSTS and TESS score in the first six months after surgery. Despite ROM after MUTARS® implant was partially limited because of surgical reasons and structural needs of the prosthesis, they found a nearly significant hip flexion ROMs increase after three months from surgery and rehabilitation. In one article [6], after intra-articular knee resection,an active extension deficit of more than 10° is reported only in 6 patients over 98 (6%).In another article [7], after extra-articular knee resection, an extensor lag > 10° was noted in 10 patients over 59 (17%) resulting in functional deficiency.

Ferrara et al. at stabilometry evaluation reported significant increase in balance at the evaluation at two and three months after surgery. The SPPB values increased (p-value 0.09) at three months and a significant increase (p-value 0.01) at six months after surgery, with better results in balance, walking time and "sit to stand" ability. Moreover, this study showed a significant increase in TESS scale (p-value 0.03) at three months after surgery.

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Activities of daily living are described only in two articles [8,12] and the results, using the KPS [8,12], ECOGG [12], scales were all good, giving an overview on the fundamental activities of daily living required for an independent care wich has possibly the highest impact on the quality of life. It is important to notice thatquality of life is investigated only in one article [10]. Pellegrino et al. demonstratedthat modular prostheses considerably improved patients'quality of life. Another important domain investigated the employability after intervention[7]. Harders J et al. demonstrated that 52% of their population worked full time after recovery and only one was not able to work at all.

*Surgical Outcomes*

Surgical complications are reported in three articles according to Henderson et al classification [1,2,6], while in one [7] are defined as major (peri-prosthetic infection, aseptic loosening, peri-prosthetic fracture) or minor (change of the bushings, wound healing disturbances).

Reducing the rate of infections has been widely studied. As known in literature [17–19], materials such as iodine, Defensive Antibacterial Coating (DAC) or Silver Coating reduce the risk of infection avoiding biofilm formation on implant surface. Pala et al. study supported this evidence, showing that silver coated MUTARS® prosthesis are related with a lower incidence of infection, even if not statistically significant, as it inhibits bacterial colonization of the prosthetic body, without toxicological side effects. Therefore, in higher risk patients, silver-coated prostheses are the preferable choice, particularly in sites such as distal femur and proximal tibia, where it prevents infections better than in other sites. They reported that infections weremore frequent in the lower limbs than in the upper limbs, with no difference in in survival to infection (p-value 0.76). They also reported that silver-coated prostheses two-stage revision and prostheses implantation, showed a lower incidence of secondary amputation compared to thetitanium implants.

Another consideration about infections comes from Hardes et al. study [7]. They found out that extra-articular knee resection, as alternative to amputation, had a higher rate of delayed wound healing and associated peri-prosthetic infections than intra-articular resection. As a consequence of peri-prosthetic infection and revisionin one case, they reportedflexion limitation of 20° in the ROM of the knee. While in 38 patientswith no infection at final follow-up themean range of flexion was 72° (10° to 100°) and a total of 25 of these had flexion of ≥ 90°.In some cases,the infection and necrosis was extensive at the point that in two patients was necessary amputation. In particular patients who received radiotherapy developed peri-prosthetic infection, as a result of delayed wound healing.This is in accordance also with the results of Hardes et al. study [6] according to whom a high BMI and administration of radiotherapy are significant risk factors for the development of wound healing disturbances.

In literature patellar tendon rupture (Type 1) is reported as a common complication inknee replacements [20]; in Bus et al. study they did not observe any patellar tendon ruptures, probably thank to the use of the attachment tube that allows for ingrowth of the extensor apparatus and apparently ensures reliable, long-lasting fixation.

They also reported that uncemented HA-coateddistal femoral replacements had a lower risk of loosening complication (Type2) (5%) than uncemented uncoated implants (31%) (p-value 0.060).

Regarding the coat, an observation comes from Kamiński et al. study. In the two groups of patients with femoral resection prostheses (tumour metastasis and implant loosening), MUTARS® stems, both press-fitcementless and cemented ones, allowed for immediate weight bearing. This is particularly important, in fact not delay to load the limb soon after theprocedure improves the patient's quality of life andfacilitates continuation of specialist treatment of the underlying disease.

Another consideration come from the study of Gosheger et al., they reported that the hexagonal-shaped design of the stem provides good rotational stability with reduced loosening rates and less stem breakage. Also, using the Trevira tube (Implantcast), that makes muscle and tendon refixation much easier, decreases dislocation and improve functional results in proximal femoral and tibia replacements.

In three articles was also evaluated the limb survival rate [4,6,7] using the Kaplan–Meier survivorship analysis. In one of these [4] 5-year limb survival rate evaluated was 87.1%. In the

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second [6] were 94.9%, 90.5% and 74.5% at one, two and ten years, respectively. In the third [7], the rate of survival of the limb was 76% at 151 months; while the rate of survival of the prosthesis without re-operation was 48% at two years and 25% at five years post-operatively

The authors of the first of these documents showed that prosthetic survival was adversely influenced by radiation therapy and chemotherapy and the second confirmed that independent significant risk factors on univariate analysis for subsequent amputationwere radiotherapy ($p = 0.041$), pathological fracture($p = 0.004$), peri-prosthetic infection ($p = 0.018$) and theuse of a reattachment tube ($p = 0.01$).

*Oncological Outcomes*

Only 4 papers [1,2,6,7] described the oncologic outcomes at follow-up. The timing of follow-up is different between the four papers: mean follow-up are 3.4 years [1], 1 year [6] and 4.7 years while median follow-up is 8.9 years [2].

We noted that, regardless of the timing of follow-up, in Pala et al. study the percentage of patients with NED is well below than other two studies [6,7]. Likewise the DWD and the AWD outcome.

Regarding overall survival at 5 and 10 years we noticed also a lower percentage of patients in Pala et al. study (58% at 5 years; 54% at 10 years) compared to Hardes et al. (84.9% at 5 years; 80.1% at 10 years). We partly explained this evidence by the mean age of the sample in the respective studies (53 vs. 18 years old).

## 5. Conclusions

In conclusion MUTARS® implantation are certainly a good alterative for patients with primary or metastatic bone tumors limb-sparing surgery. Extensive resections and prosthetic reconstructions inevitably change the alignment, biomechanics and proprioception of the affected limb, resulting for example in changes in walking patterns. MSTS score is a validate functional measure for orthopedics and oncologist but more assessments of functional outcome are needed to identify specific problems faced by patients. This information can be used to improve rehabilitation treatments and optimize patient care after limb reconstruction and achieve not only a lower rate of complications, but also satisfactory quality of life after cancer.

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