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Extraskeletal Osteosarcoma: Clinico-pathologic Features and Results of Multimodal Management

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Background

- About 1% of all soft tissue sarcomas
- First described by Wilson in 1941
- Few large series then reported
- Older individuals & usually worse survival than skeletal osteosarcoma

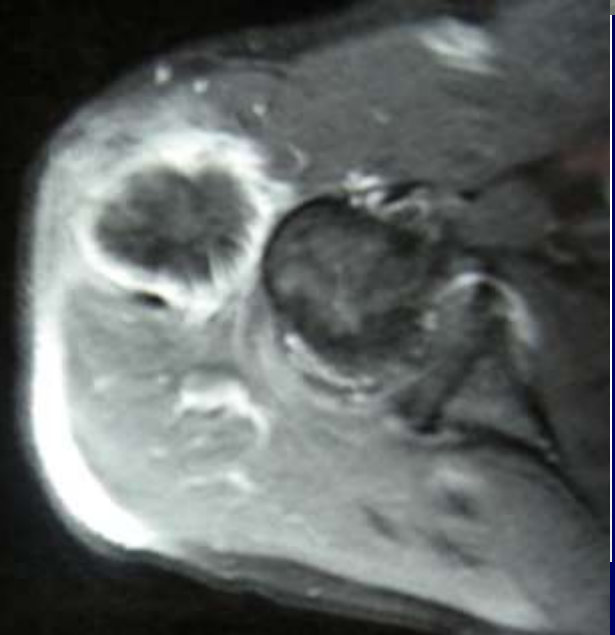


Extraskelletal Osteosarcoma

Diagnostic Criteria

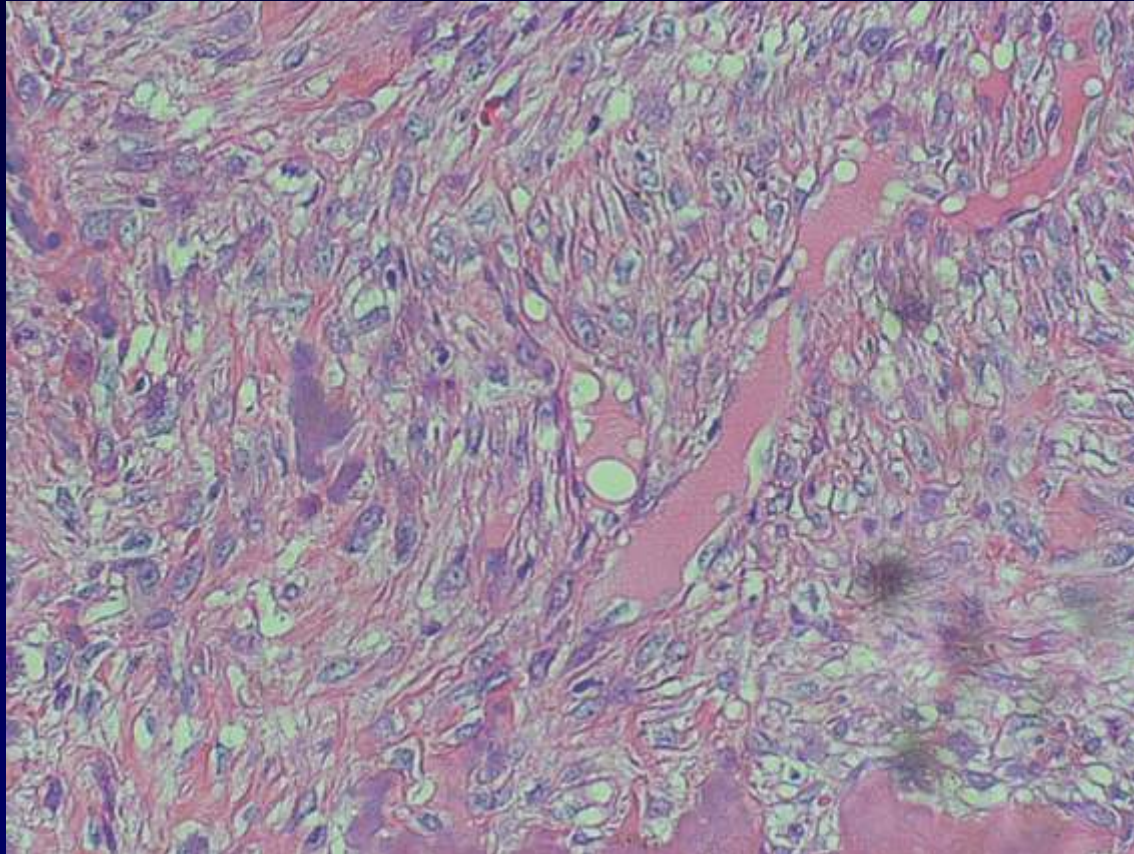


- Arise in the soft tissue and not be attached to bone/periosteum



Extraskkeletal Osteosarcoma

Diagnostic Criteria



- Uniform sarcomatous pattern, high-grade
- Produce osteoid-bone/cartilage matrix

Extraskkeletal Osteosarcoma

Classic Literature: 80's-90's

- 26-88 pts, 1915-1988, all high-grade lesions
- Mean age 51-55 yrs, M:F=1-1.9, 47-68% lower limb
- Mgmt: mostly surgical unimodal, little role for Rxt/Cht
- LR 43-69%, mets 61-80%, 5yr OS rate 24-37%
- Suggested role for tumor size, surgical margin and possibly aggressive multimodal management

MSKCC - Sordillo PP et al, Cancer, 1983

AFIP - Chung EB & Enzinger FM, Cancer, 1987

MDACC - Bane BL et al, Cancer, 1990

Mayo Clinic - Lee JS et al, Cancer, 1995



Extraskkeletal Osteosarcoma

Recent Literature

- 17-38 pts, 12-20 yrs experience, all high-grade lesions
- Mean age 44-55 yrs, M:F=1-2, 47-52% lower limb
- Mgmt: mostly multimodal - Surgery & Cht, less Rxt
- LR 16-29%, mets 7-39%, 3yr EFS 56%, 5yr EFS 47%
5ys OS rate 46-66%
- Improved outcome, better surgical margin, Cht likely beneficial even if questionable clin/path response

MDACC - Ahmad SA et al, J Clin Oncol, 2002

Munster - Goldstein-Jackson SY et al, J Cancer Res Clin Oncol, 2005

Japan, multicentric - Torigoe T et al, J Orthop Sci, 2007



Rizzoli Experience

- 48 pts, 1966-2007, 36 admitted, 12 consults
- Clinico-path & radiologic features reviewed
- Management correlated with outcome
- Updated FU obtained in all patients
- Kaplan Meier & log rank survival analysis



Rizzoli Experience

- Median age 53.6 yrs, M 21/F15, LL 69%
- Prox 52.8%, Distal 16.7%, Girdles 30.6%
- All high-grade lesions; def Dx on specimen 16 (44%)
- 23 pts localised (64%), 13 metastatic (36%)
- 16 prev. excision admitted for further surgery



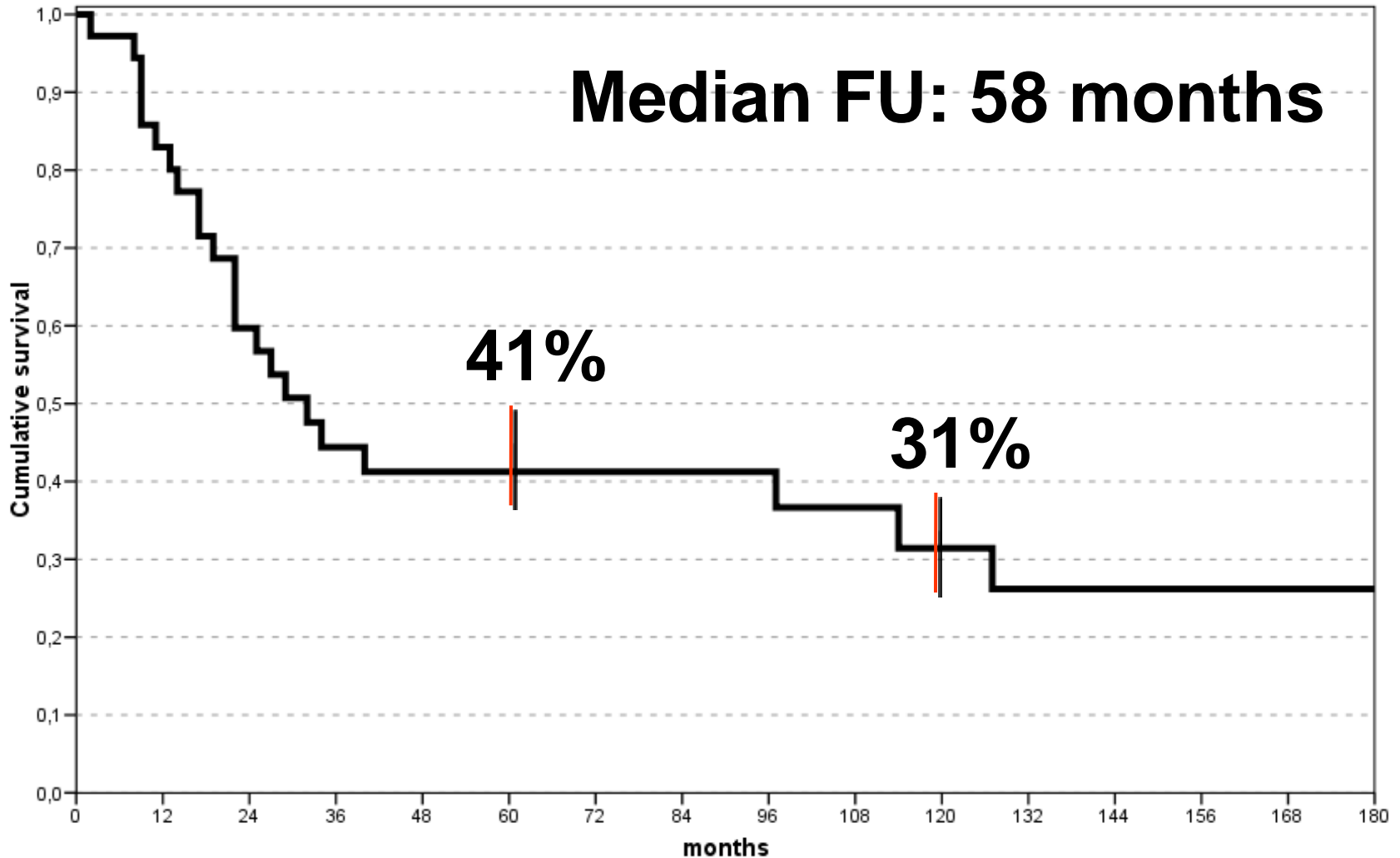
Rizzoli Experience: Management

- Surgery: 34 (LS 69.5%, amp 25%), 2 inop.
- Margins: adequate 76.5%, inadequate 23.5%
- Cht 19 (52.8%): 17 adjuv postop, 2 neoadjuv
 - 2 to 4 drugs regimen based on pt age
- Postoperative Rxt: 6 patients (16.7%)



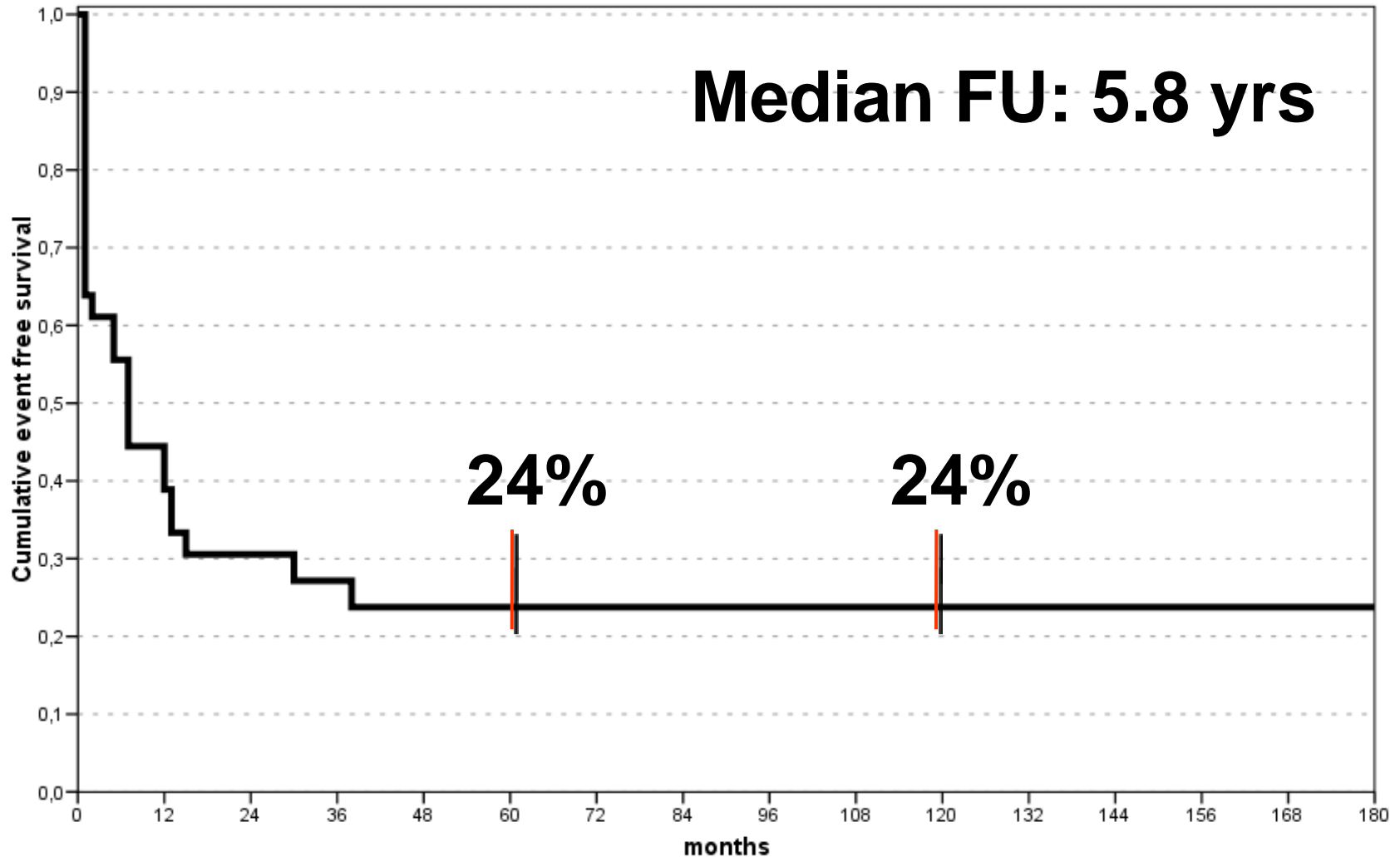
Extraskkeletal Osteosarcoma

Expected Overall Survival



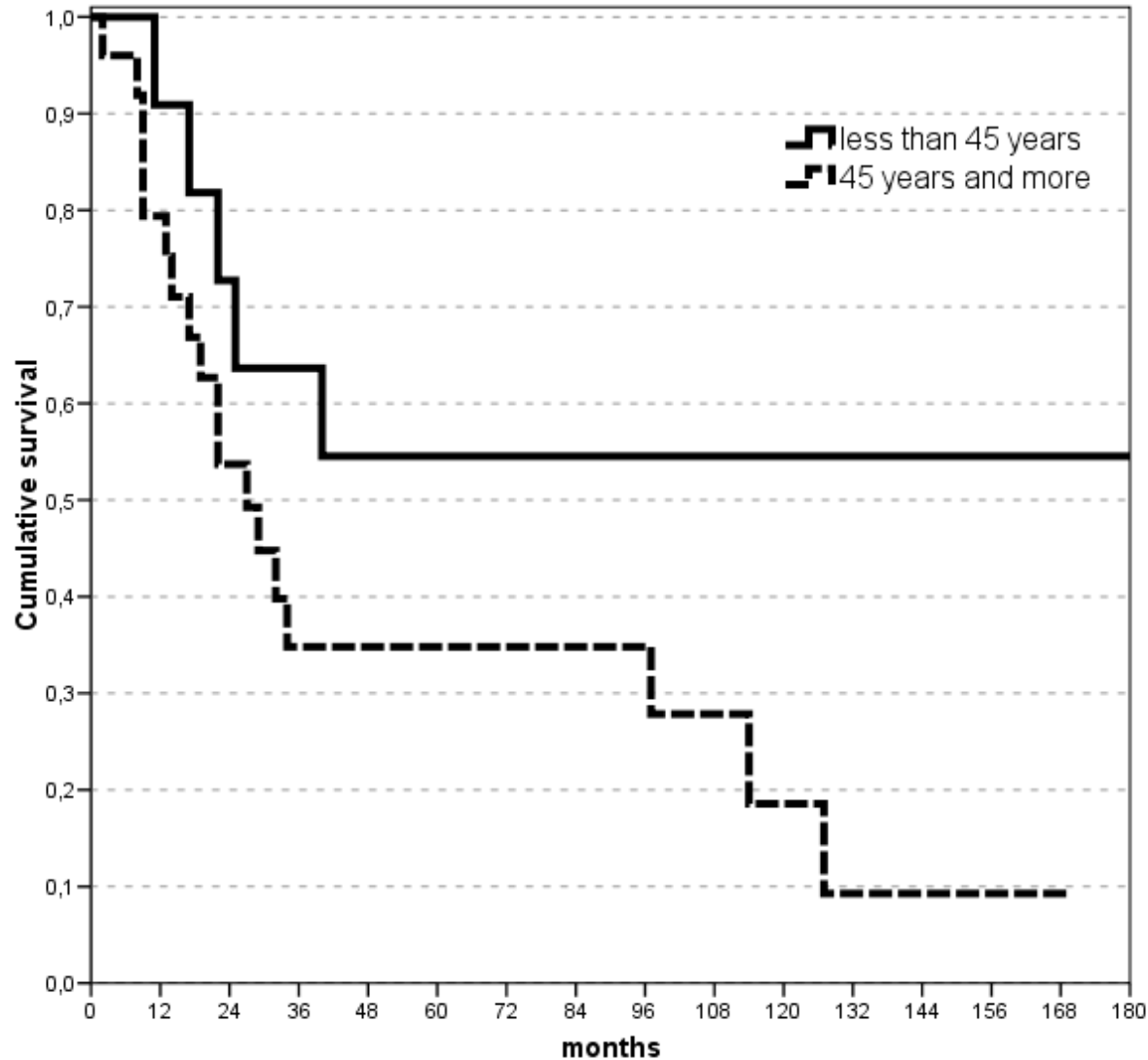
Extraskkeletal Osteosarcoma

Expected Event-Free Survival



Extraskelletal Osteosarcoma

Overall Survival: Age

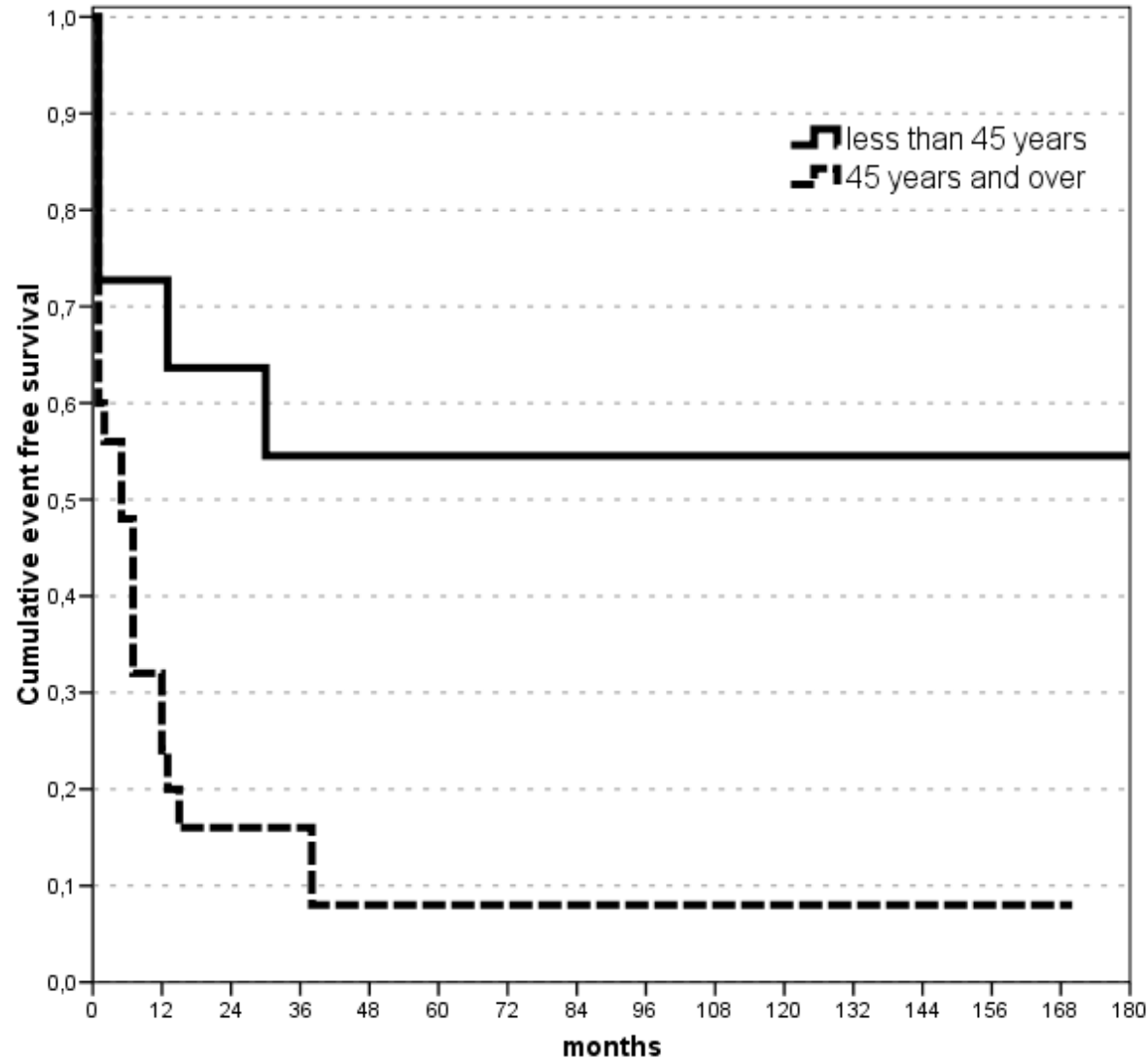


$p=0.066$



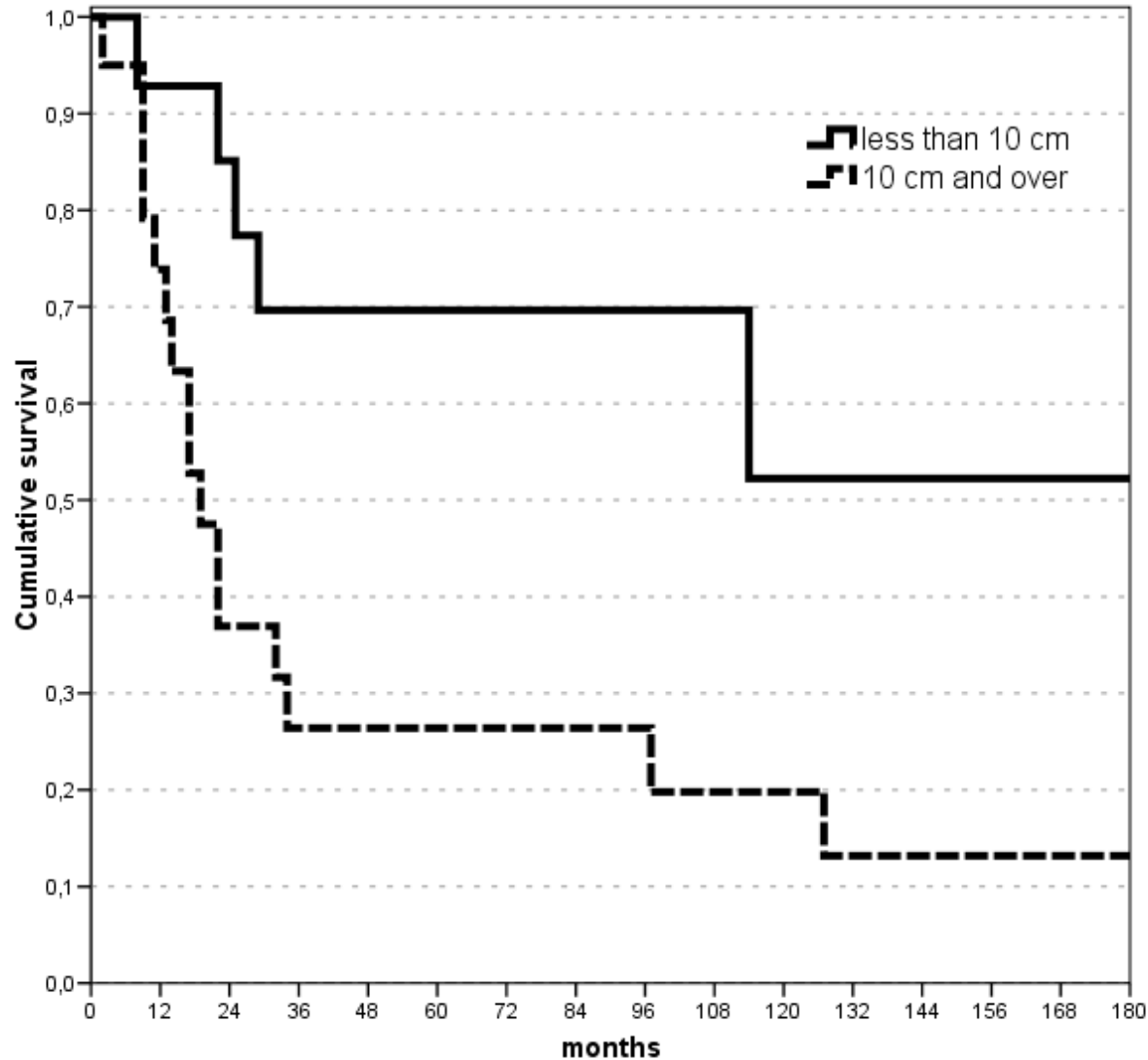
Extraskkeletal Osteosarkoma

Event-Free Survival: Age



Extraskkeletal Osteosarcoma

Overall Survival: Tumor Volume



$p=0.01$



Extraskkeletal Osteosarcoma

Overall Survival: Stage

- 23 pts localised, 9 survivors (1 DOC when DF)
 - DS survival 43.5% (DFS 39%)

NS

- 13 pts metastatic, 3 survivors (2 AWD, 1 DF)
 - DS survival 23% (DFS 7.7%)



Overall Survival: Margin and LR

- Localised 23, operated 22
 - Adequate 18, survivors 8, DFS 44.4%
 - Inadequate 4, survivors 2, DFS 50% **NS**
 - Amputation vs LS: no difference
- 8 pts developed 12 LR's → further surgery
 - 2 pts DF at final FU: 25%



Extraskkeletal Osteosarcoma

Overall Survival: Chemotherapy

- Cht: 19 pts, 8 survivors (42.1%)

NS

- No Cht: 17 pts, 5 survivors (29.4%)



Extraskelletal Osteosarcoma

Overall Survival: Chemotherapy

- Localised (23 pts) → improved DFS
 - Cht 10 pts: DFS 60%
 - No Cht 13 pts: DFS 31% (23%)

p=0.09
- Metastatic (13 pts)
 - Cht 9 pts: 1DF, 1 AWD DFS 11%
 - No Cht 4 pts: 1 AWD DFS 0%

NS



Conclusions

- Results comparable with recent literature
- Age and volume important factors
- Worse prognosis than bone OGS ?
- Biologic behavior of aggressive STS
- Cht seems valuable in pts with loc. disease



N. Fabbri
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Literature

- *Sordillo PP et al, Cancer, 1983 - MSKCC*
 - 48 pts, 1950-1982, all high-grade lesions
 - Mean age 51 yrs, M=F, 54% lower limb, 5 prev Rxt
 - Mgmt (45 pts): Surgery 43, Cht in 5 relapses
 - LR 69%, mets 80%, LR &/or mets 91%, OS 24%
 - Survivors: amput/resection & Rxt, 4/5 Cht at relapse



Literature

- *Chung EB & Enzinger FM, Cancer, 1987 - AFIP*
 - 88 pts, 1946-1982, all high-grade lesions
 - Mean age 54.6 yrs, M 58%, 46.6% lower limb
 - Management: unimodal (surgery), no details
 - 2.7 yrs mean FU on 65 pts: LR 43%, mets 63%, OS 38.4%, CDFS 12.3%
 - Better prognosis of prominent fibroblastic or MFH-like histologic component



Literature

- *Bane BL et al, Cancer, 1990 - MD Anderson CC*
 - 26 pts, 1950-1987, all high-grade lesions
 - Mean age 53.5 yrs, M:F=1.9, 61.5% lower limb
 - Dx: initial biopsy/excision not showing osteoid
 - Mgmt: Surg 9, Surg & Cht 9, Surg & Rxt 3
 - 4.6 yrs FU: LR 50%, mets 61%, NED 27%
 - Size (< 5 cm vs > 5 cm) main prognostic factor
 $p < 0.001$
 - Behaviour more like ST MFH than bone OGS



Literature

- Lee JS et al, Cancer, 1995 - Mayo Clinic
 - 40 pts, 1915-1988, all high-grade lesions
 - Mean age 50.7 yrs, M:F=1.9, 68% lower limb
 - Management: Surgery 39, Rxt 12, Cht 2
 - LR 45%, mets 65%, 5-yr survival 37%, OS 27%
 - Positive impact of radical/wide margin and chondroblastic subtype



Literature

- Ahmad SY et al, J Clin Oncol, 2002 - MD Anderson CC
 - 60 pts, 1960-99, AJCC I=3 ,II=25%, III=43%, IV=28%
 - Mean age 55 yrs, M:F=1.6, 52% lower limb
 - Management AJCC<IV: Surgery 35, Rxt 6, Cht 24
 - LR 20%, mets 40%, 5-yr survival 46%
 - 8 month survival if present with mets
 - relatively doxorubicin-resistant, poor-prognosis

ST sarcoma that is distinct from OS



Literature

- *Goldstein-Jackson SY et al, J Cancer Res Clin Oncol, 2005*
 - 17 pts, 17 insts 1986-2002, all high-grade lesions
 - Mean age 44 yrs, M:F=1.7, 47% lower limb
 - Management: Surgery 16, Rxt 1, Cht 16
 - LR 32%, mets 18%, 5-yr survival 77%
 - Positive impact of multi-agent chemotherapy



Literature

- *Torigoe T et al, J Orthop Science, 2007*
 - 20 pts, 1991-2003, UICC Stage: II=5, III=13, IV=2
 - Mean age 50 yrs, M:F=2.3, 60% lower limb
 - Management: Surgery 19, Rxt 5, Cht 15
 - LR 15%, mets 45%, 5-yr survival 66%
 - Positive impact of chemotherapy – similar findings



Rizzoli Experience

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Diagnostic Criteria



- Arise in the soft tissue and not be attached to bone/periosteum
- Polyethylene Wear & Hinge Design
- Cemented vs Uncemented Fixation
- Tendon Attachment & Soft Tissue Sealing

Extraskkeletal Osteosarcoma

Unsolved & Controversial Issues

- About 1% of all ST sarcomas
- *Wilson H, Ann Surg, 1941*



Unsolved & Controversial Issues

- Deep Infection and Septic Failure
- Polyethylene Wear & Hinge Design
- Cemented vs Uncemented Fixation
- Tendon Attachment & Soft Tissue Sealing



Musculoskeletal Tumor Advisory Forum
Rizzoli Orthopaedic Institute
Bologna, Italy
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