经典型骨肉瘤临床诊疗专家共识的解读

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【摘 要】 为了提高我国经典型骨肉瘤的诊断与治疗水平，制定一个符合我国国情、能在全国范围内实施的规范化诊治共识，中国临床肿瘤学会（CSCO）骨肉瘤专家委员会和中国抗癌协会肉瘤专业委员会组织了骨肉瘤诊治领域的相关专家，以循证医学证据为基础，综合分析并评价了国内外相关文献资料，进行了 5 次讨论和修订，最终形成了本共识，本文主要是对共识涉及的各相关内容进行解读和分析。

【关键词】 经典型骨肉瘤； 诊断； 治疗； 共识

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Interpretation of clinical practice guidelines for management of typical osteosarcoma

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【**Abstract**】 To improve the diagnosis and treatment of conventional osteosarcoma in China, we work out this consensus under the leader of Osteosarcoma Group of CSCO (Chinese Society Of Clinical Oncology) and Sarcoma Group of CACA (Chinese Anti-Cancer Association). This consensus is based on evidence-based medicine evidence with wide literature review and has been discussed and revised 5 times upon its final edition is released. This article mainly focuses on the interpretation and understanding of various aspects related to this consensus.

【**Key Words**】 Typical osteosarcoma; Diagnosis; Treatment; Consensus

1 流行病学

骨肉瘤是最常见的骨原发恶性肿瘤，年发病率约为 2 ~ 3/100 万，发病总数占人类恶性肿瘤的 0.2%，占原发骨肿瘤的 11.7%[1-6]。骨肉瘤好发于青少年，大约 75% 的患者发病年龄在 15 ~ 25 岁，中位发病年龄为 20 岁，小于 6 岁或者大于 60 岁发病相对罕见。本病男性多于女性，比例约为 1.4∶1，这种差异在 20 岁前尤为明显。大约 80% ~ 90% 的骨肉瘤发生在长管状骨，最常见的发病部位是股骨远端和胫骨近端，其次是肱骨近端，这 3 个部位大约占到所有肢体骨肉瘤的 85%[7-10]。骨肉瘤主要发生部位是干骺端，发生于骺端和骨干的病例相对罕见。

多数骨肉瘤患者的首发症状常为疼痛和肿胀，前者发生要早于后者，大约 90% 的患者在影像学上有软组织肿块，但不是都表现为局部肿胀。肺转移是最常见的转移部位[11]。历史上，截肢是治疗骨肉瘤的标准方法，仅 10% ~ 20% 的患者能够长期存活，即便存活，截肢治疗也给患者带来严重的肢体功能障碍。随着现代影像学的不断进步和外科技术的不断提高，尤其是化疗的广泛应用，骨肉瘤的综合治疗水平得到大幅度提高，骨肉瘤的保肢治疗成为趋势，5 年生存率可提高至 50% ~ 75%[12-17]。

2 预后

目前，影响骨肉瘤预后的主要因素有肿瘤部位、是否存在转移及转移部位、对化疗的组织学反应等[18-23]。发生于脊柱、骨盆等中轴骨部位的骨肉瘤预后明显差于肢体骨肉瘤，发生肺转移或其他部位转移的患者预后差，肿瘤坏死率评估结果为对化疗反应差的患者预后差[24-30]。既往骨肉瘤患者的预后极差，80% 患者因转移死亡。随着采用化疗手段，包括多种药物新辅助及辅助化疗，75% 的患者可获得长期生存，90% 的患者可以进行保肢治疗。即使是初诊时即发现有肺转移的患者，也有可能治愈。

骨肉瘤的病因和发病机制仍不明确[31-33]。病毒是可能的致病因素，原因在于动物实验研究证明病毒可诱发骨肉瘤。也有文献报道，环境中电离辐射可诱发骨肉瘤。尽管骨肉瘤患者常有创伤史，但创伤事件与骨肉瘤的发生之间是否存在因果关系还不确定。

放射治疗是继发骨肉瘤较公认的危险因素[34-39]。

3 强调多学科协作

肿瘤的诊断与治疗是一个多学科的问题，需要多学科协作，骨肉瘤也不例外。目前骨肉瘤的诊断是临床、影像、病理三者相结合，其后续治疗也涉及多个学科，因此多学科协作在骨肉瘤诊治中起重要作用[40-45]。共识推荐骨肉瘤多学科协作组的核心学科为骨肿瘤外科、骨病理科、肿瘤内科、放疗科和骨影像科，可能需要的学科为胸外科、整形外科、介入科、血管科及心理科[46]。

骨肿瘤外科、骨病理科、肿瘤内科、骨影像科和放疗科医师是骨肉瘤多学科协作团队的核心成员，是骨肉瘤治疗队伍中不可缺少的一部分，他们与骨肉瘤患者的接触最早、最密切、最频繁，在骨肉瘤患者的诊断和治疗中扮演着非常重要的角色。骨肿瘤外科、骨影像科和病理科三者相结合才能正确诊断骨肉瘤[10,47-48]。

骨肿瘤外科、肿瘤内科、放疗科分别代表了肿瘤治疗的 3 种主要方法，即外科手术、内科化疗和放射治疗。手术是骨肉瘤患者最主要的治疗方法，而化疗是骨肉瘤的重要辅助治疗手段，在骨肉瘤的综合治疗中占有重要的地位。目前骨肉瘤化疗的主要作用是提高保肢率和长期生存率，对于转移的晚期骨肉瘤患者，化疗是最主要的治疗方法。骨肉瘤是一种对放疗不敏感的肿瘤，在大剂量放疗后大多数患者仍有明显的肿瘤残存，局部控制率低，因此不能用单纯放疗来治愈骨肉瘤。放疗的作用主要是辅助性治疗或姑息治疗，对于不能手术切除的病变或拒绝截肢的患者，局部放疗有一定的作用。

骨肉瘤肺转移是制约骨肉瘤患者 5 年生存率的瓶颈之一[11]。对于发生肺转移的患者，肺转移灶应以手术切除为主，联合化疗、放疗可以使患者的生存期延长，少部分患者甚至获得长期生存，这在国内外已经基本达成共识[49-56]。骨肉瘤患者出现肺转移，如果病灶可以切除且患者的身体情况和肺功能能够耐受切除手术时，进行手术切除受累的肺组织是可以选择的治疗方式[57-58]。

骨肉瘤的治疗是一个综合过程，除常规治疗外，部分骨肉瘤患者的外科治疗需要进行皮瓣、肌瓣移植，此时需要整形外科医师的参与；在骨肉瘤化疗中，部分药物可以通过动脉灌注的形式给药，也可能需要栓塞治疗或血管造影，因此就需要介入科医师参与；当骨肉瘤侵及重要血管时，为有效实施保肢治疗，也需要血管科医师辅助进行血管移植术；对于骨肉瘤患者，尤其是青少年患者，在治疗过程中可能需经历截肢、化疗反应、手术打击等重大事件，心理科医师能够准确评估患者的心理状态，并提供适宜的心理干预，帮助他们建立治疗肿瘤的信心。

4 诊断

40 岁以下患者出现进行性的疼痛及骨病变，X 线平片上显示骨破坏、病灶边缘不清，提示恶性原发性骨肿瘤的可能性很大，应转到专业的骨肿瘤中心进一步诊断。40 岁以上患者，即使既往有恶性肿瘤病史也不能排除原发骨肉瘤的可能，同样应转诊到专业的骨肿瘤诊治中心就诊[59]。

所有疑似骨肉瘤患者的标准诊断步骤应包括：体检，原发病灶影像学检查（X 线平片、局部 MRI 和/或增强 CT 扫描），骨扫描，胸部影像学检查（胸部 CT 是发现肺转移首选的影像学检查手段），实验室检查（血常规、乳酸脱氢酶、碱性磷酸酶）；然后进行活检获得组织学诊断；最后完成骨肉瘤分期诊断。有条件者可考虑应用 PET-CT 对肿瘤进行辅助分期及疗效评估[4,8,60-63]。

4.1 临床表现 骨肉瘤的病史常为 1～3 个月，局部疼痛为早期症状，可发生在肿块出现以前，起初为间断性疼痛，渐转为持续性剧烈疼痛，尤以夜间为甚。骨端近关节处肿瘤大，硬度不一，有压痛，局部温度高，静脉扩张，有时可触及搏动，可有病理骨折[3,26,64]。

4.2 影像学表现 X 线表现为骨皮质破坏和不规则新生骨。在长管状骨，多发生于干骺端。CT 可显示骨破坏状况和肿瘤内部矿化程度，强化后可显示肿瘤的血运状况、肿瘤与血管的关系以及在骨与软组织中的范围。MRI 对软组织显示清楚，对术前计划非常有用，可显示肿瘤在软组织内侵及范围、骨髓腔内侵及范围，发现跳跃病灶。CT 或 MRI 确定的肿瘤范围的精确性已被手术切除标本所证实，因此 CT 或 MRI 是骨肉瘤影像学检查的必要手段。CT 可以较好地显示皮质破坏的界限以及三维解剖情况[61-62,65-68]。与 CT 相比，MRI 在显示肿瘤软组织侵犯方面更具优势，能精确显示肿瘤与邻近肌肉、皮下脂肪、关节以及主要神经血管束的关系。另外，MRI 可以很好地显示病变远近端的髓腔情况，

以及发现有无跳跃转移[69-72]。在某些情况下，也可以选择数字减影血管造影（DSA）检查明确血管与肿瘤的关系。

4.3 实验室检查 实验室检查如乳酸脱氢酶、碱性磷酸酶与骨肉瘤诊断及预后相关，应在患者接受新辅助化疗前进行，在化疗的过程中须监测血常规及肝肾功能。需要注意的是，这些实验室检查在治疗和随访期间应定期复查[73-75]。

4.4 病理学检查 组织学表现符合骨肉瘤定义，即原发于髓腔内的高度恶性肿瘤，肿瘤细胞可产生骨样组织。该定义说明两个问题：其一，肿瘤起源于髓腔，并且是高度恶性肿瘤；其二，肿瘤细胞能够产生骨样组织，不计量的多少[1,30]。

当病变的临床和影像学表现都提示为比较典型的骨肉瘤时，常用穿刺活检确诊[76-79]。外科治疗前须行活检术，一般来说，没有遵循适当的活检程序可能导致不良的治疗结局。活检位置选择对以后的保肢手术非常重要，穿刺点必须位于最终手术的切口线部位，以便最终手术时能够切除穿刺道，因此建议在拟行外科治疗的医院由最终手术医师或其助手进行活检术。活检时注意避免骨折，推荐进行带芯针吸活检（core needle biopsy），穿刺活检失败后可行切开活检。尽量避免切除活检，不推荐冰冻活检。细针活检（finc needle biopsy）在某些骨肿瘤中心也作为常规的活检诊断方法，但需要有经验的病理科医师配合。活检应尽量获得较多的组织，以便病理科进行常规的病理检查，还可以对新鲜标本进行分子生物学分析[80-82]。

4.5 分期 目前临床上使用最为广泛的分期系统是 Enneking 提出的外科分期系统[83]，此分期系统与肿瘤预后有很好的相关性，被美国骨骼肌肉系统肿瘤协会（Musculoskeletal Tumor Society, MSTS）及国际保肢协会采纳，又称 MSTS 外科分期。此系统根据肿瘤的组织学级别（低度恶性：Ⅰ期；高度恶性：Ⅱ期）和局部累及范围（A：间室内；B：间室外）对局限性恶性骨肿瘤进行分期，肿瘤的间室状态取决于肿瘤是否突破骨皮质；出现远隔转移（M_1）的患者为Ⅲ期（表 1）。

临床上肿瘤内科医生更为熟悉的分期系统是 2010 年美国癌症联合委员会提出的 TNM 分期系统[84]（表 2）。该系统按照肿瘤大小（T）、累及区域（N）、远处转移（M）和病理学分级（G）进行分类。

表 1 Enneking 外科分期

分期	分级	部位	转移
ⅠA	G_1	T_1	M_0
ⅠB	G_1	T_2	M_0
ⅡA	G_2	T_1	M_0
ⅡB	G_2	T_2	M_0
ⅢA	$G_{1\sim2}$	T_1	M_1
ⅢB	$G_{1\sim2}$	T_2	M_1

表 2 美国癌症联合委员会（AJCC）骨肉瘤 TNM 分期系统（第 7 版）

原发肿瘤（T）	
T_X	原发肿瘤无法评估
T_0	无原发肿瘤证据
T_1	肿瘤最大径小于或等于 8cm
T_2	肿瘤最大径大于 8cm
T_3	原发部位的不连续肿瘤
区域淋巴结（N）	
N_X	区域淋巴结不能评价
N_0	无区域淋巴结转移
N_1	区域淋巴结转移
远处转移（M）	
M_0	无远处转移
M_1	远处转移
M_{1a}	肺转移
M_{1b}	其它远处转移
病理学分级（G）	
G_X	不能估价病理学分级
G_1	高分化
G_2	中度分化
G_3	低分化
G_4	未分化
分期	
ⅠA 期	$G_X, G_{1,2}, T_1, N_0, M_0$
ⅠB 期	$G_X, G_{1,2}, T_2, N_0, M_0$
	$G_X, G_{1,2}, T_3, N_0, M_0$
ⅡA 期	$G_{3,4}, T_1, N_0, M_0$
ⅡB 期	$G_{3,4}, T_2, N_0, M_0$
Ⅲ期	$G_{3,4}, T_3, N_0, M_0$
ⅣA 期	任何 G，任何 T，N_0，M_{1a}
ⅣB 期	任何 G，任何 T，N_1，任何 M
	任何 G，任何 T，任何 N，M_{1b}

5 治疗与随访

目前骨肉瘤治疗通常采用术前化疗-外科手术-

术后化疗即新辅助化疗加手术的综合治疗模式，治疗也强调多学科协作[85-89]。

5.1 辅助化疗 尽管 20 世纪 60 年代就有学者进行试验性骨肉瘤化疗，但直到同年代 Rosen、Jaffe 等相继将这些药物联合用于骨肉瘤的术后治疗，骨肉瘤的辅助化疗（术后化疗）才真正拉开了序幕[40,56]。多中心骨肉瘤协作组（Multi-Institutional Osteosarcoma Study, MIOS）和加州大学洛杉矶医院（University of California, Los Angeles, UCLA）进行了前瞻性的随机对照研究证实另外辅助化疗的确切疗效，辅助化疗组和单纯手术组的 2 年生存率分别为 63% 和 12%（$P<0.01$）[90]。此后，众多数据均显示了辅助化疗能够显著提高患者生存率[12,90-110]，其主要原因在于化疗能够杀灭肺微小转移灶或者延迟肺转移灶出现的时间。目前观点认为：（1）术前化疗疗效好的患者，术后可维持术前化疗药物种类和剂量强度；（2）术前化疗疗效不好的患者，则需更换药物或加大剂量强度。建议骨肉瘤患者术后化疗维持总的药物剂量强度，用药时间为 8 ~ 12 个月（12 ~ 18 个周期）。需要说明的是，国际上关于骨肉瘤的化疗方案众多，包括多个版本的 T 方案[110-111]、不同历史时期的 COSS 方案[108,112] 和 Rizzoli 方案[12,113-114] 等等。尽管不同的治疗中心采用的具体方案各异，但由于使用类似的药物种类和剂量强度，其治疗效果相似。因此，本版共识并未推荐化疗方案，只强调药物种类和剂量强度。应注意的是骨肉瘤化疗剂量大、毒性高，各治疗中心均曾出现因化疗毒副作用从而导致患者死亡的情况。因此，应根据各自的情况和条件，合理调整骨肉瘤化疗的剂量强度，以保障患者的治疗安全。

5.2 新辅助化疗 20 世纪 70 年代，随着辅助化疗的疗效被进一步肯定，骨肉瘤的外科技术也有了快速的发展，使得一部分患者可以接受人工假体置换，从而避免截肢。但人工假体的个体化设计和生产在当时大约需要 2 ~ 3 个月的时间，Rosen 等[111] 为避免患者在等待手术这段时间无治疗，设计了一个术前化疗方案 T5，即给予甲氨蝶呤（200mg/kg）、长春新碱（15mg/m^2）和多柔比星（45mg/m^2）化疗，每种药物循环一次后手术，这就是最早的新辅助化疗方案。后续美国儿童肿瘤协作组（Pediatric Oncology Group, POG）也设计了一项随机对照研究[115]，一组为诊断后立即手术，另一组患者术前接受新辅助化疗，结果显示两组患者的生存率没有差异。同样，德奥肉瘤协作组（The Cooperative Osteosarcoma Study Group, COSS）[112] 和 Sloan Kettering 纪念肿瘤中心的回顾性分析均证实，是否进行新辅助化疗并不影响生存率。另外，同样基于该研究结果，对于不能保肢的患者，则可以直接进行广泛外科边界以上的截肢手术治疗，后再行化疗，患者的总生存率未因没有行术前化疗而受到影响。目前观点认为，新辅助化疗并不能在辅助化疗的基础上提高生存率，但至少有以下优点：（1）化疗期间有足够的时间进行保肢手术设计；（2）诱导肿瘤细胞凋亡，促使肿瘤边界清晰化，使得外科手术更易于进行；（3）有效的新辅助化疗可以有效地降低术后复发率，使得保肢手术可以更安全地进行[12,113,116-135]。对于术前化疗后仍不能切除的肿瘤，可行放射治疗。骨肉瘤术前化疗推荐药物为大剂量甲氨蝶呤、异环磷酰胺、阿霉素和顺铂[136-137]，给药方式可考虑序贯用药或联合用药，每例患者选用两种以上药物，经动脉或静脉给药（MTX、IFO 不适合动脉给药）。我们推荐药物剂量的范围：甲氨蝶呤 8 ~ 10g/m^2（2w），异环磷酰胺 15g/m^2（3w），阿霉素 90mg/m^2（3w），顺铂 120 ~ 140mg/m^2（2w），用药时间达 4 ~ 6 周期（2 ~ 3 个月）[138]。广泛切除术术后病理证实疗效好的患者，术后应继续术前化疗方案；广泛切除术术后病理证实疗效不好的患者，术后应改变化疗方案或增加剂量强度[123-124,139]。

5.3 新辅助化疗的疗效评估 骨肉瘤患者术前需评估新辅助化疗疗效，从临床表现、肢体周径变化可以获取化疗疗效好坏的初步判断，后续需通过影像学检查（X 线：肿瘤的表现及累及范围变化；CT：骨破坏程度变化；MRI：肿瘤局部累及范围、卫星灶、跳跃转移变化；骨扫描：范围及浓集度变化；PET-CT：肿瘤局部累及范围及骨外病灶变化）来进一步评估。术前化疗反应好表现为症状减轻、影像学上肿瘤界限变清晰、骨化更完全、肿块缩小和核素浓集减低。

骨肉瘤化疗疗效的评价包括了临床症状及体征、影像学、实验室检查和组织病理学等多方面的综合评定，其中最重要的是组织病理学对肿瘤坏死率的评估。研究人员以术后标本中肿瘤细胞的构成和坏死情况为基础，制定了多种病理评分标准，但都有一定的主观性，而且结果受取材部位的影响，因此要求多点、足量取材。关于肿瘤坏死率评估的具体技术方法和标准，文献报道各个中心不尽

相同，其中 Huvos 评级系统是至今应用最为广泛的方法（表 3）[109]。肿瘤坏死率Ⅲ～Ⅳ级者为化疗反应好，推荐术后化疗采用与术前相同的化疗方案；肿瘤坏死率Ⅰ～Ⅱ级者为化疗反应差，提示远期预后差，术后应改变术前的化疗方案；术前化疗疗效持续不佳的患者应考虑外科手术治疗。由于挽救化疗（salvage chemotherapy）的疗效一直无严格的随机对照临床试验证实，因此尽管肿瘤坏死率评估有意义，但其临床价值明显小于科研价值。同时，由于中国国情，目前在国内广泛开展肿瘤坏死率评估是不现实的，因此其应用并没有在本版共识中详述。

表 3 Huvos 的评级系统

Ⅰ级：几乎未见化疗所致的肿瘤坏死
Ⅱ级：化疗获轻度有效，肿瘤组织坏死率 > 50%，尚存有肿瘤活组织
Ⅲ级：化疗获部分有效，肿瘤组织坏死率 > 90%，部分组织切片上可见残留的肿瘤活组织
Ⅳ级：所有组织切片未见肿瘤活组织

5.4 外科治疗

5.4.1 手术方式的选择 四肢骨肉瘤的外科治疗方式通常分为截肢和保肢两种。

在 20 世纪 70 年代以前，由于局部复发率高且瘤段截除后缺乏有效的重建方法，临床上常采用截肢术，直至现在，截肢仍然是治疗骨肉瘤的重要手段之一，包括经骨截肢和关节离断术。截肢的优点在于能够最大限度地切除原发病灶，手术操作简单，无需特别技术及设备，而且费用低廉，术后并发症少，术后可以尽快进行化疗以及其他辅助治疗控制和杀灭原发病灶以外的转移。截肢的适应证包括患者要求截肢、化疗无效的ⅡB 期肿瘤、重要血管神经束受累、缺乏保肢后骨或软组织重建条件和预计义肢功能优于保肢[1,27,140-144]。

目前大约 90% 的患者可接受保肢治疗。保肢适应证包括ⅡA 期肿瘤、化疗有效的ⅡB 期肿瘤、重要血管神经束未受累、软组织覆盖完好和预计保留肢体功能优于义肢。远隔转移不是保肢的禁忌证，因此对于Ⅲ期肿瘤也可以进行保肢治疗，甚至可以行姑息性保肢治疗。但是需要引起重视的是，化疗反应好仍然是保肢治疗的前提。

保肢手术包括肿瘤切除和功能重建两个步骤。对应的是骨肿瘤学所涵盖的两部分内容，即肿瘤学和骨科学。在对骨肉瘤的治疗上也要满足肿瘤学及骨科学两方面的要求，即完整、彻底地切除肿瘤（细胞学意义上的去除肿瘤）及重建因切除肿瘤所造成的股骨肌肉系统功能病损（骨及软组织的重建）。普通骨科医师最常犯的错误是过分地重视肢体功能的保留及重建，而忽略了肿瘤的治疗，即以牺牲肿瘤治疗的外科边界为代价，保留维持良好功能所需的组织解剖结构。骨肉瘤的生物学行为是影响肢体是否保留和生存期长短的主要因素，而骨骼肌肉系统功能的优劣则影响患者的生存质量。如果肿瘤复发，其后果不仅仅是增加再截肢的风险以及加重患者的痛苦和医疗费用负担，它还使复发患者的肺转移率远远高于无复发患者，而绝大部分骨肉瘤患者死亡都是因为出现肺转移[97,118]。因此，只有保证生存，才能够考虑生存质量的好坏；倘若生存无法保证，再完美的功能也只是空谈。

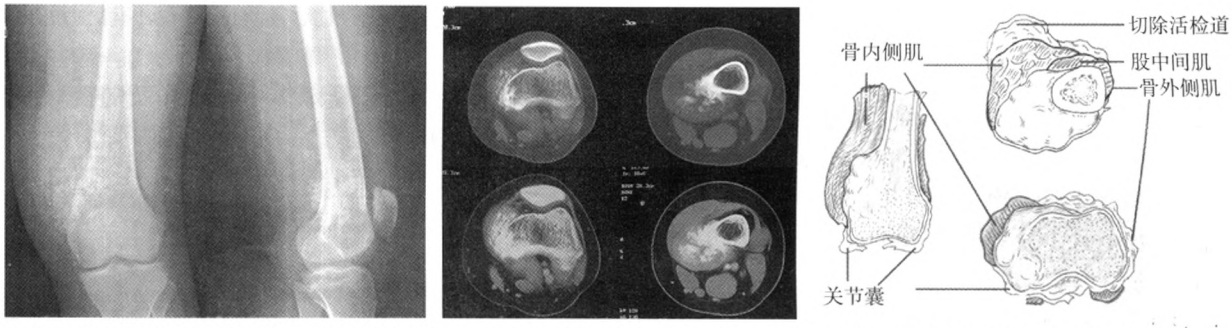
保肢手术的重建方法包括骨重建与软组织重建。骨重建即重建支撑及关节功能，软组织重建则是为了修复动力、提供良好的软组织覆盖。按照重建的特点又可以分为生物重建和非生物重建[1,47,123,139,143,145-146]。目前临床上可供选择的重建方法有：（1）人工假体，可以提供足够的稳定性和强度，允许早期负重行走，目前组配式假体功能良好，易于操作，但人工假体最主要的问题仍然是松动、感染和机械性损坏。（2）异体骨关节移植，既往的骨肉瘤治疗中曾经起过重要的作用，即使是现在，如果掌握好适应证，仍然是比较好的重建方法。其最大优点是可以提供关节表面、韧带和肌腱附着，但缺点是并发症的发生率高。有报道，包括感染、骨折等在内的并发症发生率高达 40% ～50%。（3）人工假体-异体骨复合体（APC），一般认为可以结合人工假体和异体骨两者的特点，肢体功能恢复快，但同样也结合了两种重建方式的缺点。（4）游离的带血管蒂腓骨或髂骨移植。（5）瘤段灭活再植术，该重建方式在历史上曾经广泛应用，在特定的历史时期发挥了很大的作用，但由于肿瘤灭活不确切、复发率高、无法进行术后化疗评估，并且死骨引起的并发症高，目前已基本弃用。（6）可延长式人工假体，适宜儿童患者，须定期实行延长手术。（7）旋转成型术，适宜于儿童患者，但年龄较大的患者容易存在心理接受方面的问题。无论是截肢还是保肢，术后都应积极进行康复训练。

5.4.2 外科治疗的术前计划和术后评估 不管采取什么手术方法，外科手术切除的原则仍然是以最大限

度上减少局部复发为首要目标，其次是最大限度地减少对功能的影响[147]。广泛切除意味着手术切缘为组织学阴性，以达到最佳的局部控制效果。对部分病例而言，截肢可能是达到这一目标的最适当的选择。然而，能够合理保全功能时，应首选保肢手术[148-149]。

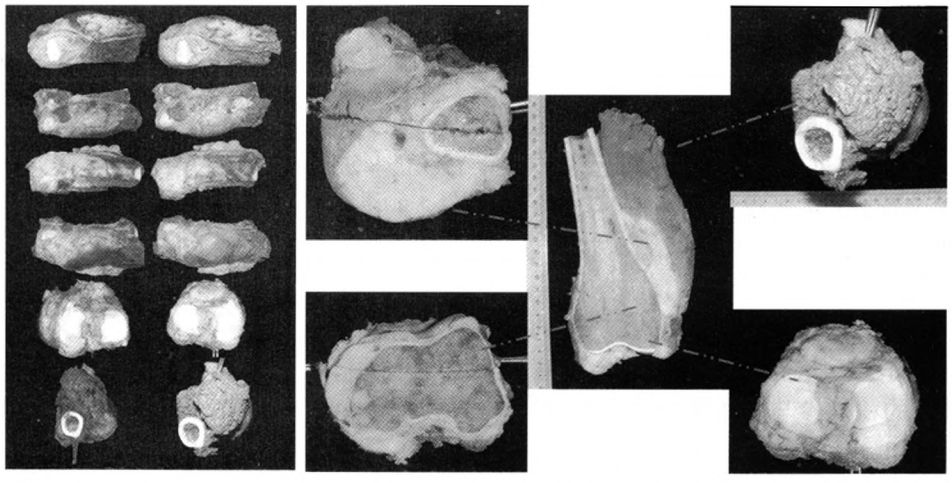
在骨肉瘤的外科治疗中，一系列关于保肢治疗的处置方法最为人们所接受，并且在术前设计时首先被考虑。虽然在不同的专家之间，保肢治疗的方法可能存在相当大的差异，但对于外科切除，确实需要一个统一的评价标准。Enneking 第一个提出这个问题，并提出了外科边界评价的概念。然而，这个标准不够细化。Kawaguchi 对此进行了进一步研究[150]，在术前化疗后根据影像学的检查结果，判断肿瘤的具体位置、大小及其与重要解剖结构的关系，从而设计肿瘤切除所需要的外科边界，即所要切除的正常软组织及截骨长度（图 1）。按照术前的设计实施手术后，要对切下的肿瘤进行外科边界的评价，以确定手术实际所达到的外科边界（图 2、图 3）。外科边界评定需要既对新鲜的、也对福尔马林浸泡过的标本进行评定。在标本的纵向和横向切面上拍摄边界最小处的照片，并且仔细地绘图。同时，对危险部位取材送病理检验，但是应注意减少福尔马林固定所引起的标本变形。

在这个评价方法中，外科边界分成 4 类：治愈性边界、广泛性边界、边缘性边界和囊内边界。



A:左股骨下端骨肉瘤伴明显骨破坏(化疗前X线平片)　B:软组织肿块明显(CT扫描)　C:术前外科治疗计划模式图(横向、纵向)

图 1　骨肉瘤表现



A：拍摄标本像从上向下分别为：前面、后面、内侧面、外侧面、近端、远端。左侧为新鲜标本，右侧为福尔马林处理过的标本

B：术后对标本进行多截面研究，评价边界

图 2　骨肉瘤手术标本

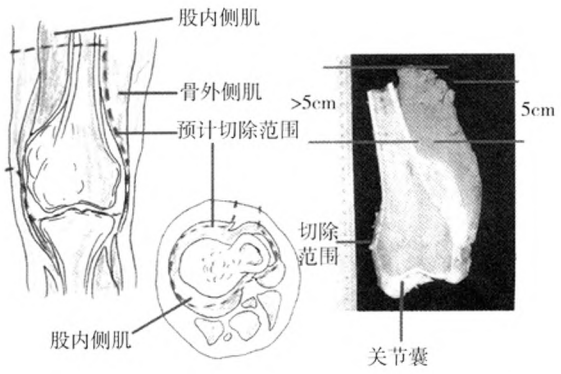


图 3 术前计划与术后标本边界评定对比

5.5 随访 由于存在复发、转移、化疗或放疗相关合并症的危险，长期随访是必要的。长期生存患者还需要注意手术的潜在并发症以及放疗或化疗的潜在副作用，如假体松动、心脏毒性、不育、继发恶性肿瘤等[10,151-152]。为了解患者生存状态，应安排一个多学科小组进行随访。治疗结束后即应开始随访。本共识推荐的随访时间间隔具体为：手术后最初 2 年，每 3 个月 1 次；第 3 年，每 4 个月 1 次；第 4、5 年，每 6 个月 1 次；5 年后每年 1 次至术后 10 年。每次随访的内容包括：全面体检、局部 X 线、骨扫描、胸部影像学检查（胸部 CT）和功能评分。

对于复发的骨肉瘤患者，建议行手术治疗，术后再次进行化疗。通常认为：对于复发时间间隔小于术后 1 年的患者，建议换二线化疗；复发时间间隔超过 1 年者可考虑原一线方案化疗；术后边缘阳性者，如果能够接受手术可考虑行扩大切除或截肢术，如果不能接受手术可考虑行局部放疗。

对于进展期骨肉瘤患者建议进行姑息性切除或截肢，不能切除者应进行放疗，即使有远隔转移也应考虑手术治疗，并强烈建议加入临床试验研究。支持治疗是晚期患者多采用的治疗方案。转移性骨肉瘤的二线治疗是骨肉瘤化疗的难点，长期生存率不足 20%[153]，目前，对于骨肉瘤肺转移的治疗强调多学科协作，至少需要骨肿瘤外科、肿瘤内科及胸外科医师的积极参与。如果化疗有效，对肺转移瘤进行外科切除是非常必要的。

但到目前为止，国际上尚无标准的骨肉瘤二线治疗方案，因此，在我国进行多中心随机对照临床试验，研究有效的二线治疗方案对于提高骨肉瘤的总体治疗水平非常重要。

6 小 结

骨肉瘤是青少年最常见的骨原发恶性肿瘤，规范的治疗模式是术前化疗-外科手术-术后化疗。骨肉瘤的诊断与治疗强调多学科协作，怀疑为骨肉瘤的患者应转诊至骨肿瘤专科医师就诊，需要接受规范化的新辅助化疗。对于接受外科手术治疗的骨肉瘤患者，应该进行术前计划，术中需严格实施，术后进行外科边界和化疗效果的评估，治疗结束后仍需长期的随访。

当前对于我国骨肉瘤的诊断治疗迫切需要解决的是规范化问题，而国际上的热点是如何在现有基础上进一步提高生存率，提高患者生活质量。目前治疗肺癌、乳腺癌、肾癌的新药层出不穷，不论是化疗药物还是靶向药物，均使患者有不同程度的受益[154-155]，也极大地鼓舞了医师的士气。这些研究成果，很多是得益于全球多中心合作及随机对照临床试验的开展。为了进一步提高我国骨肉瘤的诊治水平，在我国进行骨肉瘤多中心协作、随机对照的临床试验迫在眉睫。

参考文献

[1] Picci P. Osteosarcoma (osteogenic sarcoma) [J]. Orphanet J Rare Dis, 2007, 2: 6.

[2] Chou AJ, Geller DS, Gorlick R. Therapy for osteosarcoma: where do we go from here? [J]. Pediatr Drugs, 2008, 10(5): 315 - 327.

[3] Meyers PA, Gorlick R. Osteosarcoma [J]. Pediatr Clin North Am, 1997, 44(4): 973 - 989.

[4] Ta HT, Dass CR, Choong PFM, et al. Osteosarcoma treatment: state of the art [J]. Cancer Metastasis Rev, 2009, 28(1-2): 247 - 263.

[5] 李 昕，李建民，杨志平. ⅡB 期骨肉瘤临床预后相关因素分析（附 40 例报告）[J]. 山东医药，2006，46(3)：6 - 8.

[6] 谭平先，雍碧城，沈靖南，等. 413 例骨肉瘤化疗、手术和预后的 10 年随访研究 [J]. 中国骨科临床与基础研究杂志，2011，3(4)：256 - 262.

[7] Ritter J, Bielack SS. Osteosarcoma [J]. Ann Oncol, 2010, 21 (Suppl 7): 320 - 325.

[8] Geller DS, Gorlick R. Osteosarcoma: a review of diagnosis, management, and treatment strategies [J]. Clin Adv Hematol Oncol, 2010, 8(10): 705 - 718.

[9] Messerschmitt PJ, Garcia RM, Abdul-Karim FW, et al. Osteosarcoma [J]. J Am Acad Orthop Surg, 2009, 17(8): 515 - 527.

[10] Saeter G. Osteosarcoma: ESMO clinical recommendations for diagnosis, treatment and follow-up [J]. Ann Oncol, 2007, 18 (Suppl 2): 77 - 78.

[11] Marcove RC, Martini N, Rosen G. The treatment of pulmonary metastasis in osteogenic sarcoma[J]. Clin Orthop Relat Res, 1975, 111: 65-70.

[12] Bacci G, Longhi A, Fagioli F, et al. Adjuvant and neoadjuvant chemotherapy for osteosarcoma of the extremities: 27 year experience at Rizzoli Institute, Italy[J]. Eur J Cancer, 2005, 41(18): 2836-2845.

[13] Taylor WF, Ivins JC, Pritchard DJ, et al. Trends and variability in survival among patients with osteosarcoma: a 7-year update[J]. Mayo Clin Proc, 1985, 60(2): 91-104.

[14] Taylor WF, Ivins JC, Dahlin DC, et al. Trends and variability in survival from osteosarcoma[J]. Mayo Clin Proc, 1978, 53(11): 695-700.

[15] Pan KL, Chan WH, Ong GB, et al. Limb salvage in osteosarcoma using autoclaved tumor-bearing bone[J]. World J Surg Oncol, 2012, 10(1): 105.

[16] Dunham WK. Osteogenic sarcoma treated with limb salvage[J]. Ala Med, 1983, 53(5): 29-35.

[17] Pochanugool L, Nontasut S, Subhadharaphandou T, et al. Multidisciplinary "limb salvage" treatment of osteosarcoma[J]. J Med Assoc Thai, 1991, 74(9): 404-411.

[18] Bentzen SM. Prognostic factor studies in oncology: osteosarcoma as a clinical example[J]. Int J Radiat Oncol Biol Phys, 2001, 49(2): 513-518.

[19] Raymond AK, Chawla SP, Carrasco CH, et al. Osteosarcoma chemotherapy effect: a prognostic factor[J]. Semin Diagn Pathol, 1987, 4(3): 212-236.

[20] Juergens H, Kosloff C, Nirenberg A, et al. Prognostic factors in the response of primary osteogenic sarcoma to preoperative chemotherapy (high-dose methotrexate with citrovorum factor)[J]. Natl Cancer Inst Monogr, 1981, 56: 221-226.

[21] Harting MT, Lally KP, Andrassy RJ, et al. Age as a prognostic factor for patients with osteosarcoma: an analysis of 438 patients[J]. J Cancer Res Clin Oncol, 2010, 136(4): 561-570.

[22] Sami SH, Rafati AH, Hodjat P. Tissue necrosis after chemotherapy in osteosarcoma as the important prognostic factor[J]. Saudi Medical J, 2008, 29(8): 1124-1129.

[23] Hagleitner MM, Hoogerbrugge PM, van der Graaf WT, et al. Age as prognostic factor in patients with osteosarcoma[J]. Bone, 2011, 49(6): 1173-1177.

[24] 牛晓辉, 王 涛, 李 远, 等. 骨肉瘤区域淋巴结检查的临床意义[J]. 中国骨肿瘤骨病, 2005, 4(3): 131-132, 153.

[25] Bakhshi S, Radhakrishnan V. Prognostic markers in osteosarcoma[J]. Expert Rev Anticancer Ther, 2010, 10(2): 271-287.

[26] Bramer JAM, van Linge JH, Grimer RJ, et al. Prognostic factors in localized extremity osteosarcoma: a systematic review[J]. Eur J Surg Oncol, 2009, 35(10): 1030-1036.

[27] Bielack S, Jürgens H, Jundt G, et al. Osteosarcoma: the COSS experience[J]. Cancer Treat Res, 2009, 152: 289-308.

[28] Arceci RJ. Response in osteosarcoma. Information you can't use ···yet? [J]. J Pediatr Hematol Oncol, 2003, 25(11): 837-838.

[29] Bielack SS, Kempf-Bielack B, Delling G, et al. Prognostic factors in high-grade osteosarcoma of the extremities or trunk: an analysis of 1,702 patients treated on neoadjuvant cooperative osteosarcoma study group protocols[J]. J Clin Oncol, 2002, 20(3): 776-790.

[30] Ferguson WS, Goorin AM. Current treatment of osteosarcoma[J]. Cancer Invest, 2001, 19(3): 292-315.

[31] Kansara M, Thomas DM. Molecular pathogenesis of osteosarcoma[J]. DNA Cell Biol, 2007, 26(1): 1-18.

[32] Wang LL. Biology of osteogenic sarcoma[J]. Cancer J, 2005, 11(4): 294-305.

[33] Fuchs B, Pritchard DJ. Etiology of osteosarcoma[J]. Clin Orthop Relat Res, 2002, 397: 40-52.

[34] Finkel MP, Jr. Reilly CA, Biskis BO. Pathogenesis of radiation and virus-induced bone tumors[J]. Recent Results Cancer Res, 1976, 54: 92-103.

[35] Ziewacz JE, Song JW, Blaivas M, et al. Radiation-induced meningeal osteosarcoma of tentorium cerebelli with intradural spinal metastases[J]. Surg Neuro Int, 2010, 1: 14.

[36] Mavrogenis AF, Pala E, Guerra G, et al. Post-radiation sarcomas. Clinical outcome of 52 patients[J]. J Surg Oncol, 2012, 105(6): 570-576.

[37] Patel AJ, Rao VY, Fox BD, et al. Radiation-induced osteosarcomas of the calvarium and skull base[J]. Cancer, 2011, 117(10): 2120-2126.

[38] Kadota Y, Utsumi T, Inoue M, et al. Radiation-induced osteosarcoma 17 years after mediastinal irradiation following surgical removal of thymoma[J]. Gen Thorac Cardiovasc Surg, 2010, 58(12): 651-653.

[39] Franco Gutiérrez V, Llorente Pendá JL, Coca Pelaz A, et al. Radiation-induced sarcomas of the head and neck[J]. J Craniofac Surg, 2008, 19(5): 1287-1291.

[40] Jaffe N, Traggis D, Cassady JR, et al. Multidisciplinary treatment for macrometastatic osteogenic sarcoma[J]. Br Med J, 1976, 2(6043): 1039-1041.

[41] Jaffe N, Murray J, Traggis D, et al. Multidisciplinary treatment for childhood sarcoma[J]. Am J Surg, 1977, 133(4): 405-413.

[42] Jr. Douglass HO. Osteosarcoma: survival gains resulting from multidisciplinary therapy[J]. Prog Clin Cancer, 1978, 7: 83-96.

[43] Calvo FA, Ortiz de Urbina D, Sierrasesumaga L, et al. Intraoperative radiotherapy in the multidisciplinary treatment of bone sarcomas in children and adolescents[J]. Med Pediatr Oncol, 1991, 19(6): 478-485.

[44] Delépine N, Delépine G, Desbois JC, et al. Osteogenic osteosarcoma: a model of curable disease by multidisciplinary approach of treatment[J]. Biom Pharmacother, 1990, 44(5): 243-248.

[45] Calvo FA, Sierrasesumaga L, Martin I, et al. Intraoperative radiotherapy in the multidisciplinary treatment of pediatric tumors.

A preliminary report on initial results[J]. Acta Oncol, 1989, 28(2): 257 - 260.

[46] Federman N, Bernthal N, Eilber FC, et al. The multidisciplinary management of osteosarcoma[J]. Curr Treat Options Oncol, 2009, 10(1 - 2): 82 - 93.

[47] Jaffe N. Osteosarcoma: review of the past, impact on the future. The American experience[J]. Cancer Treat Res, 2009, 152: 239 - 262.

[48] Fletcher BD. Imaging pediatric bone sarcomas-Diagnosis and treatment-related issues[J]. Radiol Clin North Am, 1997, 35(6): 1477 - 1494.

[49] Anderson P, Salazar-Abshire M. Improving outcomes in difficult bone cancers using multimodality therapy, including radiation: physician and nursing perspectives[J]. Curr Oncol Rep, 2006, 8(6): 415 - 422.

[50] Baeza MR, Barkley HT, Jr. Fernandez CH. Total-lung irradiation in the treatment of pulmonary metastases[J]. Radiology, 1975, 116(1): 151 - 154.

[51] Briccoli A, Rocca M, Salone M, et al. High grade osteosarcoma of the extremities metastatic to the lung: long-term results in 323 patients treated combining surgery and chemotherapy, 1985 - 2005[J]. Surg Oncol, 2010, 19(4): 193 - 199.

[52] Cupps RE, Ahmann DL, Soule EH. Treatment of pulmonary metastatic disease with radiation therapy and adjuvant actinomycin D. Preliminary observations[J]. Cancer, 1969, 24(4): 719 - 723.

[53] Hamada H, Aoki Y, Yoshikawa H, et al. Treatment for osteosarcoma-a study of thirty-two patients treated with systemic chemotherapy and radical surgery[J]. Nihon Seikeigeka Gakkai Zasshi, 1986, 60(1): 73 - 83.

[54] Putnam JB Jr, Roth JA. Surgical treatment for pulmonary metastases from sarcoma[J]. Hematol Oncol Clin North Am, 1995, 9(4): 869 - 887.

[55] Rosen G, Tefft M, Martinez A, et al. Combination chemotherapy and radiation therapy in the treatment of metastatic osteogenic sarcoma[J]. Cancer, 1975, 35(3): 622 - 630.

[56] Rosenburg SA, Flye MW, Conkle D, et al. Treatment of osteogenic sarcoma. II. Aggressive resection of pulmonary metastases[J]. Cancer treatment reports, 1979, 63(5): 753 - 756.

[57] Siegel HJ, Pressey JG. Current concepts on the surgical and medical management of osteosarcoma[J]. Expert Rev Anticancer Ther, 2008, 8(8): 1257 - 1269.

[58] Marulanda GA, Henderson ER, Johnson DA, et al. Orthopedic surgery options for the treatment of primary osteosarcoma[J]. Cancer Control, 2008, 15(1): 13 - 20.

[59] 张 清, 徐万鹏, 郭 卫, 等. 我国骨肉瘤治疗现状及改进建议-17 家骨肿瘤治疗中心 1992 - 2008 年资料分析[J]. 中国骨肿瘤骨病, 2009, 8(3): 129 - 132.

[60] Nagarajan R, Weigel BJ, Thompson RC, et al. Osteosarcoma in the first decade of life[J]. Med Pediatric Oncol, 2003, 41(5): 480 - 483.

[61] Ferrari S, Balladelli A, Palmerini E, et al. Imaging in bone sarcomas. The chemotherapist's point of view[J/OL]. Eur J Radiol, 2011 [2012 - 08 - 10]. http://www.ncbi.nlm.nih.gov/pubmed/22209429.

[62] Errani C, Kreshak J, Ruggieri P, et al. Imaging of bone tumors for the musculoskeletal oncologic surgeon[J/OL]. Eur J Radiol, 2011 [2012 - 08 - 10]. http://www.ncbi.nlm.nih.gov/pubmed/22209430.

[63] Eftekhari F. Imaging assessment of osteosarcoma in childhood and adolescence: diagnosis, staging, and evaluating response to chemotherapy[J]. Cancer Treat Res, 2009, 152: 33 - 62.

[64] Craft AW. Osteosarcoma: the European Osteosarcoma Intergroup (EOI) perspective[J]. Cancer Treat Res, 2009, 152: 263 - 74.

[65] Guo J, Reddick WE, Glass JO, et al. Dynamic contrast-enhanced magnetic resonance imaging as a prognostic factor in predicting event-free and overall survival in pediatric patients with osteosarcoma[J]. Cancer, 2012, 118(15): 3776 - 3785.

[66] Wetzel LH, Levine E, Murphey MD. A comparison of MR imaging and CT in the evaluation of musculoskeletal masses[J]. Radiographics, 1987, 7(5): 851 - 874.

[67] Sundaram M, McGuire MH, Herbold DR. Magnetic resonance imaging of osteosarcoma[J]. Skeletal Radiol, 1987, 16(1): 23 - 29.

[68] Aisen AM, Martel W, Braunstein EM, et al. MRI and CT evaluation of primary bone and soft-tissue tumors[J]. AJR Am J Roentgenol, 1986, 146(4): 749 - 756.

[69] Meyer JS, Nadel HR, Marina N, et al. Imaging guidelines for children with Ewing sarcoma and osteosarcoma: a report from the Children's Oncology Group Bone Tumor Committee[J]. Pediatr Blood Cancer, 2008, 51(2): 163 - 170.

[70] Reddick WE, Wang S, Xiong X, et al. Dynamic magnetic resonance imaging of regional contrast access as an additional prognostic factor in pediatric osteosarcoma[J]. Cancer, 2001, 91(12): 2230 - 2237.

[71] Sundaram M, McGuire MH, Herbold DR, et al. Magnetic resonance imaging in planning limb-salvage surgery for primary malignant tumors of bone[J]. J Bone Joint Surg Am, 1986, 68(6): 809 - 819.

[72] Wallack ST, Wisner ER, Werner JA, et al. Accuracy of magnetic resonance imaging for estimating intramedullary osteosarcoma extent in pre-operative planning of canine limb-salvage procedures[J]. Vet Radiol Ultrasound, 2002, 43(5): 432 - 441.

[73] Pochanugool L, Subhadharaphandou T, Dhanachai M, et al. Prognostic factors among 130 patients with osteosarcoma[J]. Clin Orthop Relat Res, 1997, 345: 206 - 214.

[74] Bacci G, Dallari D, Battistini A, et al. The prognostic value of serum alkaline phosphatase in osteosarcoma of the limbs[J]. Chir Organi Mov, 1992, 77(2): 171 - 180.

[75] Bacci G, Picci P, Ferrari S, et al. Prognostic significance of serum alkaline phosphatase measurements in patients with osteosarcoma treated with adjuvant or neoadjuvant chemotherapy[J].

Cancer, 1993, 71(4): 1224 - 1230.

[76] Kilpatrick SE, Ward WG, Bos GD, et al. The role of fine needle aspiration biopsy in the diagnosis and management of osteosarcoma[J]. Pediatr Pathol Mol Med, 2001, 20(3): 175 - 187.

[77] Agarwal S, Agarwal T, Agarwal R, et al. Fine needle aspiration of bone tumors[J]. Cancer Detect Prev, 2000, 24(6): 602 - 609.

[78] Ward WG Sr, Kilpatrick S. Fine needle aspiration biopsy of primary bone tumors[J]. Clin Orthop Relat Res, 2000, 373: 80 - 87.

[79] Nanda M, Rao ES, Behera KC, et al. Fine needle aspiration cytology (FNAC) in malignant bone tumours[J]. Indian J Pathol Microbiol, 1994, 37(3): 247 - 253.

[80] Raymond AK, Simms W, Ayala AG. Osteosarcoma specimen management following primary chemotherapy[J]. Hematol Oncol Clin North Am, 1995, 9(4): 841 - 867.

[81] Hudson TM, Schiebler M, Springfield DS, et al. Radiologic imaging of osteosarcoma: role in planning surgical treatment[J]. Skeletal Radiol, 1983, 10(3): 137 - 146.

[82] Delling G, Krumme H, Salzer-Kuntschik M. Morphological changes in osteosarcoma after chemotherapy--COSS 80[J]. J Cancer Res Clin Oncol, 1983, 106 (Suppl): 32 - 37.

[83] Wolf RE, Enneking WF. The staging and surgery of musculoskeletal neoplasms[J]. Orthop Clin North Am, 1996, 27(3): 473 - 481.

[84] Wunder JS, Healey JH, Davis AM, et al. A comparison of staging systems for localized extremity soft tissue sarcoma[J]. Cancer, 2000, 88(12): 2721 - 2730.

[85] Ogura K, Goto T, Imanishi J, et al. Neoadjuvant and adjuvant chemotherapy with modified mesna, adriamycin, ifosfamide, and decarbazine (MAID) regimen for adult high-grade non-small round cell soft tissue sarcomas[J/OL]. Int J Clin Oncol, 2011[2012 - 08 - 20]. http://www.ncbi.nlm.nih.gov/pubmed/22179493.

[86] Machak GN, Tkachev SI, Solovyev YN, et al. Neoadjuvant chemotherapy and local radiotherapy for high-grade osteosarcoma of the extremities[J]. Mayo Clin Proc, 2003, 78(2): 147 - 155.

[87] Lowery MA, Cadoo K, Treacy A, et al. Neoadjuvant chemotherapy for adult osteosarcoma: Results of long term follow-up[J]. J Clin Oncol, 2008, 26(15 Suppl): a 10543.

[88] 胡永成. 全国骨肉瘤化疗座谈会纪要[J]. 中华骨科杂志, 1999, 19(1): 7 - 10.

[89] 蔡楠伯, 牛晓辉, 张 清, 等. 肢体原发成骨肉瘤综合治疗的远期结果[J]. 中华外科杂志, 2000, 38(5): 329 - 331.

[90] Link MP, Goorin AM, Horowitz M, et al. Adjuvant chemotherapy of high-grade osteosarcoma of the extremity. Updated results of the Multi-Institutional Osteosarcoma Study[J]. Clin Orthop Relat Res, 1991, 270: 8 - 14.

[91] Anninga JK, Gelderblom H, Fiocco M, et al. Chemotherapeutic adjuvant treatment for osteosarcoma: where do we stand?[J]. Eur J Cancer, 2011, 47(16): 2431 - 2445.

[92] Zalupski MM, Rankin C, Ryan JR, et al. Adjuvant therapy of osteosarcoma--A Phase II trial: Southwest Oncology Group study 9139[J]. Cancer, 2004, 100(4): 818 - 825.

[93] Bacci G, Longhi A, Ferrari S, et al. Prognostic factors in nonmetastatic Ewing's sarcoma tumor of bone: an analysis of 579 patients treated at a single institution with adjuvant or neoadjuvant chemotherapy between 1972 and 1998[J]. Acta Oncol, 2006, 45(4): 469 - 475.

[94] Bacci G, Picci P, Ferrari S, et al. Primary chemotherapy and delayed surgery for non-metastatic telangiectatic osteosarcoma of the extremities. Results in 28 patients[J]. Eur J Cancer, 1994, 30A(5): 620 - 626.

[95] Bramwell VH. The role of chemotherapy in the management of non-metastatic operable extremity osteosarcoma[J]. Semin Oncol, 1997, 24(5): 561 - 571.

[96] Bush H. Adjuvant chemotherapy: an approach to the management of *malignant disease*[J]. *Bri* J Hosp Med, 1978, 20(3): 260 - 275.

[97] Campanacci M, Bacci G, Bertoni F, et al. The treatment of osteosarcoma of the extremities: twenty years experience at the Istituto Ortopedico Rizzoli[J]. Cancer, 1981, 48(7): 1569 - 1581.

[98] Cortes EP, Holland JF. Adjuvant chemotherapy for primary osteogenic sarcoma[J]. Surg Clin North Am, 1981, 61(6): 1391 - 1404.

[99] Craft AW, Machin D, Souhami RL. Adjuvant chemotherapy for non-metastatic osteosarcoma of the extremities in two New Zealand cancer centres[J]. Aust N Z J Med, 1996, 26(2): 230.

[100] Donaldson SS. The value of adjuvant chemotherapy in the management of sarcomas in children[J]. Cancer, 1985, 55(9 Suppl): 2184 - 2197.

[101] Eilber F, Giuliano A, Eckardt J, et al. Adjuvant chemotherapy for osteosarcoma: a randomized prospective trial[J]. J Clin Oncol, 1987, 5(1): 21 - 26.

[102] Eilber FR, Rosen G. Adjuvant chemotherapy for osteosarcoma[J]. Semin Oncol, 1989, 16(4): 312 - 322.

[103] Frei E 3rd, Jaffe N, Gero M, et al. Adjuvant chemotherapy of osteogenic sarcoma: progress and perspectives[J]. J Natl Cancer Inst, 1978, 60(1): 3 - 10.

[104] Goorin AM, Frei E 3rd, Abelson HT. Adjuvant chemotherapy for osteosarcoma: a decade of experience[J]. Surg Clin North Am, 1981, 61(6): 1379 - 1389.

[105] Hazan EJ, Hornicek FJ, Tomford W, et al. The effect of adjuvant chemotherapy on osteoarticular allografts[J]. Clin Orthop Relat Res, 2001, 385: 176 - 181.

[106] Jaffe N. Adjuvant chemotherapy in osteosarcoma: an odyssey of rejection and vindication[J]. Cancer Treat Res, 2009, 152: 219 - 237.

[107] Jaffe N, Smith D, Jaffe MR, et al. Intraarterial cisplatin in the management of stage IIB osteosarcoma in the pediatric and adolescent age group[J]. Clin Orthop Relat Res, 1991, 270: 15 - 21.

[108] Winkler K, Beron G, Kotz R, et al. Adjuvant chemotherapy in os-

teosarcoma-effects of cisplatinum, BCD, and fibroblast interferon in sequential combination with HD-MTX and adriamycin. Preliminary results of the COSS 80 study[J]. J Cancer Res Clin Oncol, 1983, 106 (Suppl): 1 - 7.

[109] Rosen G, Marcove RC, Huvos AG, et al. Primary osteogenic sarcoma: eight-year experience with adjuvant chemotherapy[J]. J Cancer Res Clin Oncol, 1983, 106 (Suppl): 55 - 67.

[110] Meyers PA, Heller G, Healey J, et al. Chemotherapy for nonmetastatic osteogenic sarcoma: the Memorial Sloan-Kettering experience[J]. J Clin Oncol, 1992, 10(1): 5 - 15.

[111] Rosen G, Marcove RC, Caparros B, et al. Primary osteogenic sarcoma: the rationale for preoperative chemotherapy and delayed surgery[J]. Cancer, 1979, 43(6): 2163 - 2177.

[112] Bielack SS, Kempf-Bielack B, Heise U, et al. Combined modality treatment for osteosarcoma occurring as a second malignant disease. Cooperative German-Austrian-Swiss Osteosarcoma Study Group[J]. J Clin Oncol, 1999, 17(4): 1164.

[113] Bacci G, Briccoli A, Ferrari S, et al. Neoadjuvant chemotherapy for osteosarcoma of the extremity: long-term results of the Rizzoli's 4th protocol[J]. Eur J Cancer, 2001, 37(16): 2030 - 2039.

[114] Bacci G, Ferrari S, Mercuri M, et al. Neoadjuvant chemotherapy for extremity osteosarcoma--preliminary results of the Rizzoli's 4th study[J]. Acta Oncol, 1998, 37(1): 41 - 48.

[115] Goorin AM, Schwartzentruber DJ, Devidas M, et al. Presurgical chemotherapy compared with immediate surgery and adjuvant chemotherapy for nonmetastatic osteosarcoma: Pediatric Oncology Group Study POG-8651[J]. J Clin Oncol, 2003, 21(8): 1574 - 1580.

[116] Bacci G, Balladelli A, Palmerini E, et al. Neoadjuvant chemotherapy for osteosarcoma of the extremities in preadolescent patients: the Rizzoli Institute experience[J]. J Pediatr Hematol Oncol, 2008, 30(12): 908 - 912.

[117] Bacci G, Bertoni F, Longhi A, et al. Neoadjuvant chemotherapy for high-grade central osteosarcoma of the extremity. Histologic response to preoperative chemotherapy correlates with histologic subtype of the tumor[J]. Cancer, 2003, 97(12): 3068 - 3075.

[118] Bacci G, Briccoli A, Rocca M, et al. Neoadjuvant chemotherapy for osteosarcoma of the extremities with metastases at presentation: recent experience at the Rizzoli Institute in 57 patients treated with cisplatin, doxorubicin, and a high dose of methotrexate and ifosfamide[J]. Ann Oncol, 2003, 14(7): 1126 - 1134.

[119] Bacci G, Ferrari S, Bertoni F, et al. Neoadjuvant chemotherapy for peripheral malignant neuroectodermal tumor of bone: recent experience at the istituto rizzoli[J]. J Clin Oncol, 2000, 18(4): 885 - 892.

[120] Bacci C, Ferrari S, Bertoni F, et al. Neoadjuvant chemotherapy for osseous malignant fibrous histiocytoma of the extremity: results in 18 cases and comparison with 112 contemporary osteosarcoma patients treated with the same chemotherapy regimen[J]. J Chemother, 1997, 9(4): 293 - 299.

[121] Bacci G, Ferrari S, Longhi A, et al. Relationship between dose-intensity of treatment and outcome for patients with osteosarcoma of the extremity treated with neoadjuvant chemotherapy[J]. Oncol Rep, 2001, 8(4): 883 - 888.

[122] Bacci G, Forni C, Ferrari S, et al. Neoadjuvant chemotherapy for osteosarcoma of the extremity: intensification of preoperative treatment does not increase the rate of good histologic response to the primary tumor or improve the final outcome[J]. J Pediatr Hematol Oncol, 2003, 25(11): 845 - 853.

[123] Bacci G, Lari S. Adjuvant and neoadjuvant chemotherapy in osteosarcoma[J]. Chir Organi Mov, 2001, 86(4): 253 - 268.

[124] Bacci G, Longhi A, Forni C, et al. Neoadjuvant chemotherapy for radioinduced osteosarcoma of the extremity: The Rizzoli experience in 20 cases[J]. Int J Radiat Oncol Biol Phys, 2007, 67(2): 505 - 511.

[125] Bacci G, Mercuri M, Longhi A, et al. Neoadjuvant chemotherapy for the treatment of osteosarcoma of the extremities: a comparison of results obtained in single-institution and multicenter trials[J]. Chir Organi Mov, 2004, 89(4): 283 - 292.

[126] Bacci G, Mercuri M, Ruggieri P, et al. Neoadjuvant chemotherapy for malignant fibrous histiocytoma of bone and for osteosarcoma of the limbs: a comparison between the results obtained for 21 and 144 patients, respectively, treated during the same period with the same chemotherapy protocol[J]. Chir Organi Mov, 1996, 81(2): 139 - 153.

[127] Bacci G, Picci P, Ferrari S, et al. Neoadjuvant chemotherapy for nonmetastatic osteosarcoma of the extremities: the recent experience at the Rizzoli Institute. [J]. Cancer Treat Res, 1993, 62: 299 - 308.

[128] Bacci G, Picci P, Ferrari S, et al. Neoadjuvant chemotherapy for the treatment of osteosarcoma of the extremities: excellent response of the primary tumor to preoperative treatment with methotrexate, cisplatin, adriamycin, and ifosfamide. Preliminary results[J]. Chir Organi Mov, 1995, 80(1): 1 - 10.

[129] Bacci G, Picci P, Ruggieri P, et al. Neoadjuvant chemotherapy for the treatment of osteosarcoma of the limbs. Preliminary results in 100 patients treated preoperatively with high doses of methotrexate i. v. followed by cisplatin (i. a.) and adriamycin [J]. Chir Organi Mov, 1991, 76(1): 1 - 16.

[130] Cassano WF, Graham-Pole J, Dickson N. Etoposide, cyclophosphamide, cisplatin, and doxorubicin as neoadjuvant chemotherapy for osteosarcoma[J]. Cancer, 1991, 68(9): 1899 - 1902.

[131] Graham-Pole J, Ayass M, Cassano W, et al. Neoadjuvant chemotherapy for patients with osteosarcoma: University of Florida studies[J]. Cancer Treat Res, 1993, 62: 339 - 346.

[132] Nakano H, Tateishi A, Imamura T, et al. Intensive preoperative chemotherapy for osteosarcoma in the lower extremity[J]. Anticancer Res, 1998, 18(4B): 2859 - 2864.

[133] Uchida A, Myoui A, Araki N, et al. Neoadjuvant chemotherapy for pediatric osteosarcoma patients[J]. Cancer, 1997, 79(2): 411 - 415.

[134] Wada T, Isu K, Takeda N, et al. A preliminary report of neoadjuvant chemotherapy NSH-7 study in osteosarcoma: preoperative salvage chemotherapy based on clinical tumor response and the use of granulocyte colony-stimulating factor [J]. Oncology, 1996, 53(3): 221 - 227.

[135] Wynendaele W, van Oosterom AT. Neoadjuvant/primary chemotherapy in cancer treatment: what advantage? [J]. Forum (Genova), 1999, 9(3): 212 - 221.

[136] 郭 卫, 杨荣利, 汤小东, 等. 成骨肉瘤新辅助化学药物治疗的疗效分析[J]. 中华医学杂志, 2004, 84 (14): 1186 - 1190.

[137] 王 臻, 黄耀添, 黄鲁豫, 等. 高危骨肉瘤的临床特点及治疗对策[J]. 第四军医大学学报, 2002, 23(5): 465 - 468.

[138] 牛晓辉, 蔡橒伯, 张 清, 等. ⅡB期肢体骨肉瘤189例综合治疗临床分析[J]. 中华外科杂志, 2005, 43(24): 1576 - 1579.

[139] Uchida A, Myoui A, Araki N, et al. Neoadjuvant chemotherapy for pediatric osteosarcoma patients[J]. Cancer, 1997, 79(2): 411 - 415.

[140] Wittig JC, Bickels J, Priebat D, et al. Osteosarcoma: a multidisciplinary approach to diagnosis and treatment[J]. Am Fam Physician, 2002, 65(6): 1123 - 1132.

[141] Bielack S, Jürgens H, Jundt G, et al. Pediatric and adolescent osteosarcoma[M]. Springer US, 2010: 125 - 145.

[142] Bacci G, Picci P, Ruggieri P, et al. Primary chemotherapy and delayed surgery (neoadjuvant chemotherapy) for osteosarcoma of the extremities. The Istituto Rizzoli Experience in 127 patients treated preoperatively with intravenous methotrexate (high versus moderate doses) and intraarterial cisplatin[J]. Cancer, 1990, 65(11): 2539 - 2553.

[143] Scully SP, Temple HT, O'Keefe RJ, et al. The surgical treatment of patients with osteosarcoma who sustain a pathologic fracture [J]. Clin Orthop Relat Res, 1996, 324: 227 - 232.

[144] Ferrari S, Palmerini E, Staals EL, et al. The treatment of nonmetastatic high grade osteosarcoma of the extremity: review of the Italian Rizzoli experience. Impact on the future [J]. Cancer Treat Res, 2009, 152: 275 - 287.

[145] Bacci G, Ferrari S, Longhi A, et al. Pattern of relapse in patients with osteosarcoma of the extremities treated with neoadjuvant chemotherapy[J]. Eur J Cancer, 2001, 37(1): 32 - 38.

[146] Dinçbaş FO, Koca S, Mandel NM, et al. The role of preoperative radiotherapy in nonmetastatic high-grade osteosarcoma of the extremities for limb-sparing surgery[J]. Int J Radiat Oncol Biol Phys, 2005, 62(3): 820 - 828.

[147] 牛晓辉. 恶性骨肿瘤外科治疗的术前计划及术后评估[J]. 中华外科杂志, 2007, 45(10): 699 - 701.

[148] Lascelles BD, Dernell WS, Correa MT, et al. Improved survival associated with postoperative wound infection in dogs treated with limb-salvage surgery for osteosarcoma[J]. Ann Surg Oncol, 2005, 12(12): 1073 - 1083.

[149] Li J, Wang Z, Guo Z, et al. Irregular osteotomy in limb salvage for juxta-articular osteosarcoma under computer-assisted navigation[J]. J Surg Oncol, 2012, 106(4): 411 - 416.

[150] Kawaguchi N, Ahmed AR, Matsumoto S, et al. The concept of curative margin in surgery for bone and soft tissue sarcoma[J]. Clin Orthop Relat Res, 2004, 419: 165 - 172.

[151] Fitzhugh CD, Wise B, Baird K, et al. Secondary supratentorial primitive neuroectodermal tumor following treatment of childhood osteosarcoma[J]. Pediatr Blood Cancer, 2009, 53(3): 496 - 498.

[152] Ferrari S, Bacci G, Picci P, et al. Long-term follow-up and post-relapse survival in patients with non-metastatic osteosarcoma of the extremity treated with neoadjuvant chemotherapy[J]. Ann Oncol, 1997, 8(8): 765 - 771.

[153] Bielack SS, Marina N, Ferrari S, et al. Osteosarcoma: the same old drugs or more? [J]. J Clin Oncol, 2008, 26(18): 3102 - 3103.

[154] 孙 燕. 肿瘤药物治疗百年回顾与展望[J]. 中华肿瘤杂志, 2004, 26(11): 701 - 703.

[155] 孙 燕. 临床肿瘤50年: 创新中发展[J]. 医学研究杂志, 2010, 39(4): 1 - 3.

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经典型骨肉瘤临床诊疗专家共识的解读

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参考文献(155条)

1. Picci P Osteosarcoma (osteogenic sarcoma) 2007

2. Chou AJ;Geller DS;Gorlick R Therapy for osteosarcoma:where do we go from here[外文期刊] 2008(05)

3. Meyers PA;Gorlick R Osteosarcoma[外文期刊] 1997(04)

4. Ta HT;Dass CR;Choong PFM Osteosarcoma treatment:state of the art 2009(1-2)

5. 李昕;李建民;杨志平 ⅡB期骨肉瘤临床预后相关因素分析(附40例报告)[期刊论文]-山东医药 2006(03)

6. 谭平先;雍碧城;沈靖南 413例骨肉瘤化疗、手术和预后的10年随访研究[期刊论文]-中国骨科临床与基础研究杂志 2011(04)

7. Ritter J;Bielack SS Osteosarcoma 2010(Suppl 7)

8. Geller DS;Gorlick R Osteosarcoma:a review of diagnosis,management,and treatment strategies 2010(10)

9. Messerschmitt PJ;Garcia RM;Abdul-Karim FW Osteosarcoma 2009(08)

10. Saeter G Osteosarcoma:ESMO clinical recommendations for diagnosis,treatment and follow-up 2007(Suppl 2)

11. Marcove RC;Martini N;Rosen G The treatment of pulmonary metastasis in osteogenic sarcoma 1975

12. Bacci G;Longhi A;Fagioli F Adjuvant and neoadjuvant chemotherapy for osteosarcoma of the extremities:27 year expericnce at Rizzoli Institutc,Italy[外文期刊] 2005(18)

13. Taylor WF;Ivins JC;Pritchard DJ Trends and variability in survival among patients with osteosarcoma:a 7-year update 1985(02)

14. Taylor WF;Ivins JC;Dahlin DC Trends and variability in survival from osteosarcoma 1978(11)

15. Pan KL;Chan WH;Ong GB Limb salvage in osteosarcoma using autoclaved tumor-bearing bone 2012(01)

16. Dunham WK Osteogenic sarcoma treated with limb salvage 1983(05)

17. Pochanugool L;Nontasut S;Subhadharaphandou T Multidisciplinary "limb salvage" treatment of osteosarcoma 1991(09)

18. Bentzen SM Prognostic factor studies in oncology:osteosarcoma as a clinical example 2001(02)

19. Raymond AK;Chawla SP;Carrasco CH Osteosarcoma chemotherapy effect:a prognostic factor 1987(03)

20. Juergens H;Kosloff C;Nirenberg A Prognostic factors in the response of primary osteogenic sarcoma to preoperative chemotherapy (high-dose methotrexate with citrovorum factor) 1981

21. Harting MT;Lally KP;Andrassy RJ Age as a prognostic factor for patients with osteosarcoma:an analysis of 438 patients 2010(04)

22. Sami SH;Rafati AH;Hodjat P Tissue nccrosis after chcmother apy in osteosarcoma as the important prognostic factor 2008(08)

23. Hagleitner MM;Hoogerbrugge PM;van der Graaf WT Age as prognostic factor in patients with osteosarcoma 2011(06)

24. 牛晓辉;王涛;李远 骨肉瘤区域淋巴结检查的临床意义[期刊论文]-中国骨肿瘤骨病 2005(03)

25. Bakhshi S;Radhakrishnan V Prognostic markers in osteosarcoma 2010(02)

26. Bramer JA;van Linge JH;Grimer RJ Prognostic factors in localized extremity osteosarcoma:a systematic

review 2009(10)

27. Bielack S;Jürgens H;Jundt G Osteosarcoma:the COSS experience 2009

28. Arceci RJ Response in osteosarcoma.Information you can't use …yet 2003(11)

29. Bielack SS;Kempf-Bielack B;Delling G Prognostic factors in high grade osteosarcoma of the extremitics or trunk:an a nalvsis of 1,702 patients treated on neoadjuvant cooperative osteosarcoma study group protocols [外文期刊] 2002(03)

30. Ferguson WS;Goorin AM Current treatment of osteosarcoma[外文期刊] 2001(03)

31. Kansara M;Thomas DM Molecular pathogenesis of osteosarcoma[外文期刊] 2007(01)

32. Wang LL Biology of osteogenic sarcoma 2005(04)

33. Fuchs B;Pritchard DJ Etiology of osteosarcoma 2002

34. Finkei M P,Jr;Reilly CA;Biskis BO Pathogenesis of radiation and virus-induced bone tumors 1976

35. Ziewacz JE;Song JW;Blaivas M Radiation-induced meningcal osteosarcoma of tentorium cerebelli with intradural spinal metastases 2010

36. Mavrogenis AF;Pala E;Guerra G Post-radiation sarcomas.Clinical outcome of 52 patients 2012(06)

37. Patel AJ;Rao VY;Fox BD Radiation-induced osteosarcomas of the calvarium and skull base 2011(10)

38. Kadota Y;Utsumi T;Inoue M Radiation-induced osteosarcoma 17 years after mediastinal irradiation following surgical removal of thymoma 2010(12)

39. Franco Gutiérrez V;Llorente Pendá JL;Coca Pelaz A Radiation-induced sarcomas of thc head and neck 2008(05)

40. Jaffe N;Traggis D;Cassady JR Multidisciplinary treatment for macrometastatic osteogenic sarcoma 1976(6043)

41. Jaffe N;Murray J;Traggis D Multidisciplinary treatment for childhood sarcoma 1977(04)

42. Jr.Douglass HO Osteosarcoma:survival gains resulting from multidisciplinary therapy 1978

43. Calvo FA;Ortiz de Urbina D;Sierrasesumaga L Intraoperative radiotherapy in the multidisciplinary treatment of bone sarcomas in children and adolescents 1991(06)

44. Delépine N;Delépine G;Desbois JC Osteogenie osteosarcoma:a model of curable disease by multidisciplinary approach of treatment 1990(05)

45. Calvo FA;Sierrasesumaga L;Martin I Intraoperative radiotherapy in the multidisciplinary treatment of pediatric tumors.A preliminary report on initial results 1989(02)

46. Federman N;Bernthal N;Eilber FC The multidisciplinary management of osteosarcoma 2009(1-2)

47. Jaffe N Osteosarcoma:review of the past,impact on the future.The American experience 2009

48. Fletcher BD Imaging pediatric bone sarcomas-Diagnosis and treatment-related issues 1997(06)

49. Andcrson P;Salazar Abshire M Improving outcomes in difficult bone cancers using multimodality therapy,including radiation:physician and nursing perspectives 2006(06)

50. Baeza MR;Barkley HT,Jr;Fernandez CH Total-lung irradiation in the treatment of pulmonary metastases 1975(01)

51. Briccoli A;Rocca M;Salone M High grade osteosarcoma of the extremities metastatic to the lung:long-term results in 323 patients treated combining surgery and chemotherapy.1985-2005 2010(04)

52. Cupps RE;Ahmann DL;Soule EH Treatment of pulmonary metastatic disease with radiation therapy and adjuvant Actinomycin D.Preliminary observations 1969(04)

53. Hamada H;Aoki Y;Yoshikawa H Treatment for osteosarcoma a study of thirty-two patients treated with systemic chemotherapy and radical surgery 1986(01)

54. Putnam JB Jr;Roth JA Surgical treatment for pulmonary metastases from sarcoma 1995(04)

55. Rosen G;Tefft M;Martinez A Combination chemotherapy and radiation therapy in the treatment of metastatic osteogenic sarcoma 1975(03)

56. Rosenburg SA;Flye MW;Conklc D Treatment of osteogenic sarcoma. Ⅱ. Aggressive resection of pulmonary metastascs 1979(05)

57. Siegel HJ;Pressey JG Current concepts on the surgical and medical management of osteosarcoma 2008(08)

58. Marulanda GA;Henderson ER;Johnson DA Orthopedic surgery options for the treatment of primary osteosarcoma 2008(01)

59. 张清;徐万鹏;郭卫 我国骨肉瘤治疗现状及改进建议-17家骨肿瘤治疗中心1992-2008年资料分析[期刊论文]-中国骨肿瘤骨病 2009(03)

60. Nagarajan R;Weigel BJ;Thompson RC Osteosarcoma in the first decade of life 2003(05)

61. Ferrari S;Balladelli A;Palmerini E Imaging in bone sarcomas. The chemotherapist's point of view 2011

62. Errani C;Kreshak J;Ruggieri P Imaging of bone tumors for the musculoskeletal oncologic surgeon 2011

63. Eftckhari F Imaging assessment of osteosarcoma in childhood and adolescence:diagnosis, staging, and evaluating response to chemotherapy 2009

64. Craft AW Osteosarcoma:the European Osteosarcoma Intergroup (EOI) perspective 2009

65. Guo J;Reddick WE;Glass JO Dynamic contrast-cnhanced magnetic resonance imaging as a prognostic factor in predicting event-free and overall survival in pediatric patients with osteosarcoma 2012(15)

66. Wetzel LH;Levine E;Murphey MD A comparison of MR imaging and CT in the evaluation of musculoskeletal masscs 1987(05)

67. Sundaram M;McGuire MH;Herbold DR Magnetic resonance imaging of osteosarcoma 1987(01)

68. Aisen AM;Martel W;Braunstein EM MRI and CT evaluation of primary bone and soft-tissue tumors 1986(04)

69. Meyer JS;Nadel HR;Marina N Imaging guidelines for children with Ewing sarcoma and osteosarcoma:a report from the Children's Oncology Group Bone Tumor Commiuee 2008(02)

70. Reddick WE;Wang S;Xiong X Dynamic magnetic resonance imaging of regional contrast access as an additional prognostic factor in pediatric osteosarcoma[外文期刊] 2001(12)

71. Sundaram M;McGuire MH;Herbold DR;ct al Magnetic reso nance imaging in planning limb-salvage surgery for primary malignant tumors of bone 1986(06)

72. Wallack ST;Wisner ER;Werner JA Accuracy of magnetic resonance imaging for estimating intramedullary osteosarcoma extent in pre-operative planning of canine limb-salvage procedures[外文期刊] 2002(05)

73. Pochanugool L;Subhadharaphandou T;Dhanachai M Prognostic factors among 130 patients with osteosarcoma 1997

74. Bacci G;Dallari D;Battistini A The prognostic value of serum alkaline phosphatase in osteosarcoma of the limbs 1992(02)

75. Bacci G;Picci P;Ferrari S Prognostic significance of serum alkaline phosphatase measurements in patients with osteosarcoma treated with adjuvant or ncoadjuvant chemotherapy 1993(04)

76. Kilpatrick SE;Ward WG;Bos GD The role of fine nccdle aspiration biopsy in the diagnosis and management of osteosarcoma 2001(03)

77. Agarwal S;Agarwal T;Agarwal R Finc needle aspiration of bone tumors 2000(06)

78. Ward WG Sr;Kilpatrick S Fine needle aspiration biopsy of primary bone tumors 2000

79. Nanda M;Rao ES;Behera KC Fine needle aspiration cytology (FNAC) in malignant bonc tumours 1994(03)

80. Raymond AK;Simms W;Ayala AG Osteosarcoma specimen management following primary c hcmotherapy 1995(04)

81. Hudson TM;Schiebler M;Springfield DS Radiologic imaging of osteosareoma:role in planning surgieal treatment 1983(03)

82. Delling G;Krumme H;Salzer-Kuntschik M Morphological changes in osteosarcoma after chcmothcrapy--COSS 80 1983(Suppl)

83. Wolf RE;Enneking WF The staging and surgery of musculoskeletal neoplasms 1996(03)

84. Wunder JS;Healey JH;Davis AM A comparison of staging systems for localized extremity soft tissue sarcoma 2000(12)

85. Ogura K;Goto T;Imanishi J Neoadjuvant and adjuvant chemotherapy with modified mesna,adriamycin,ifosfamide,and decarbazine (MAID) regimen for adult high-grade non-small round cell soft tissue sarcomas 2011

86. Machak GN;Tkachev SI;Solovyev YN Neoadjuvant chemotherapy and loeal radiotherapy for high-grade osteosarcoma of the extremities[外文期刊] 2003(02)

87. Lowery MA;Cadoo K;Treacy A Neoadjuvant ehemotherapy for adult osteosarcoma:Results of long term follow-up 2008(15 Suppl)

88. 胡永成 全国骨肉瘤化疗座谈会纪要[期刊论文]-中华骨科杂志 1999(01)

89. 蔡楹伯;牛晓辉;张清 肢体原发成骨肉癌综合治疗的远期结果[期刊论文]-中华外科杂志 2000(05)

90. Link MP;Goorin AM;Horowitz M Adjuvant chemotherapy of high-grade osteosarcoma of the extremity.Updated results of the Multi-Institutional Osteosarcoma Study 1991

91. Anninga JK;Gelderblom H;Fioeco M Chemotherapeutic adjuvant treatment for osteosareoma:where do we stand 2011(16)

92. Zalupski MM;Rankin C;Ryan JR Adjuvant therapy of osteosarcoma--A Phase H trial:Southwest Oneology Group study 9139[外文期刊] 2004(04)

93. Bacci G;Longhi A;Ferrari S Prognostic factors in nonmetastatic Ewing's sarcoma tumor of bone:an analysis of 579 patients treated at a single institution with adjuvant or neoadjuvant chemotherapy between 1972 and 1998[外文期刊] 2006(04)

94. Bacci G;Picci P;Ferrari S Primary chemotherapy and delayed surgery for non-metastatic tclangicctatic osteosarcoma of the extremities.Results in 28 patients 1994(05)

95. Bramwcll VH The role of chemotherapy in the management of non-ntetastatic operable extremity ostcosarcoma 1997(05)

96. Bush H Adjuvant chemotherapy:an approach to the management of malignant disease 1978(03)

97. Campanacci M;Bacei G;Bertoni F The treatment of osteosarcoma of the extremities:twenty year 's experience at the Istituto Ortopedico Rizzoli 1981(07)

98. Cortes EP;Holland JF Adjuvant chemotherapy for primary osteogenic sacoma 1981(06)

99. Craft AW;Machin D;Souhami RL Adjuvant chemotherapy for non-metastatic osteosarcoma of the extremities in two New Zealand cancer centres 1996(02)

100. [illegible] The value of adjuvant chemotherapy in the managcment of sarcomas in children 1985(9 Suppl)

101. Eilber F;Giuliano A;Eekardt J Adjuvant chemotherapy for osteosarcoma:a randomized prospective trial 1987(01)

102. Eilber FR;Rosen G Adjuvant chemotherapy for osreosarcoma 1989(04)

103. Frei E 3rd;Jaffe N;Gero M Adjuvant chemotherapy of osteogenic sarcoma:progress and perspectives 1978(01)

104. Goorin AM;Frei E 3rd;Abelson HT Adjuvant chemotherapy for osteosarcoma:a decade of experience 1981(06)

105. Hazan EJ;Hornicek FJ;Tomford W The effect of adjuvant chemotherapy on osteoarticular allografts 2001

106. Jaffe N Adjuvant chemotherapy in osteosarcoma:an odyssey of rejection and vindication 2009

107. Jaffe N;Smith D;Jaffe MR Intraarterial cisplatin in the management of stage IIB osteosarcoma in the pediatric and adolescent age group 1991

108. Winkler K;Beron G;Kotz R Adjuvant chemotherapy in osteosarcoma-effects of cisplatinum,BCD,and fibroblast intcrferon in sequential combination with HD-MTX and adriamyein.Preliminary results of the COSS 80 study 1983(Suppl)

109. Rosen G;Marcove RC;Huvos AG Primary osteogenic sarcoma:eight-year experience with adjuvant chemotherapy 1983(Suppl)

110. Meyers PA;Heller G;Healey J Chemotherapy for nonmetastatic osteogenic sarcoma:the Memorial Sloan-Kettering experience 1992(01)

111. Rosen G;Marcove RC;Caparros B Primary osteogenic sarcoma:the rationale for preoperative chemothcrapy and delayed surgery 1979(06)

112. Bielack SS;Kempf-Bielack B;Heise U Combined modality treatment for osteosarcoma occurring as a second malignant disease.Cooperative German-Austrian-Swiss Osteosarcoma Study Group[外文期刊] 1999(04)

113. Bacci G;Briccoli A;Ferrari S Neoadjuvant chemotherapy for osteosarcoma of the extremity:long-term results of the Rizzoli ’s 4th protocol 2001(16)

114. Bacci C;Ferrari S;Mercuri M Neoadjuvant chernotherapy for extremity osteosarcoma-preliminary results of the Rizzoli ’s 4th study[外文期刊] 1998(01)

115. Goorin AM;Schwartzentruber DJ;Devidas M Presurgical chemotherapy compared with immediate surgery and adjuvant chemotherapy for nonmetastatic osteosareoma:Pediatric Oncology Group Study POG-8651[外文期刊] 2003(08)

116. Bacei G;Balladelli A;Palmerini E Neoadjuvant chemotherapy for osteosarcoma of the extremities in preadolescent patients:the Rizzoli Institute experience 2008(12)

117. Bacci G;Bertoni F;Longhi A Neoadjuvant chemotherapy for high-grade central osteosarcoma of the extremitv.Histologic response to preoperative chemotherapy correlates with histologic subtype of the tumor [外文期刊] 2003(12)

118. Bacci G;Briccoli A;Rocca M Neoadjuvant chemotherapy for osteosarcoma of the extremities with metastases at presentation:recent experience at the Rizzoli Institute in 57 patients treated with cisplatin,doxorubicin,and a high dose of methotrexate and ifosfamide[外文期刊] 2003(07)

119. Bacci G;Ferrari S;Bertoni F Neoadjuvant chemotherapy for peripheral malignant ncuroectodermal tumor of bone:recent experience at the istituto rizzoli 2000(04)

120. Bacci C;Ferrari S;Bertoni F Neoadjuvant chemotherapy for osseous malignant fibrous histiocytoma of the extremities:results in 18 cases and comparison with 112 contemporary ostcosarcoma patients treated with the

same chemotherapy regimen[J 1997(04)

121. Bacci G;Ferrari S;Longhi A Relationship between doseintensity of treatment and outcome for patients with osteosarcoma of the extremity treated with neoadjuvant chcmotherapy 2001(04)

122. Bacci C;Forni C;Ferrari S Neoadjuvant chemotherapy for osteosarcoma of the extremity:intensification of preoperative treatment does not increase the rate of good histologic response to the primary tumor or improve the final outeome 2003(11)

123. Bacci G;Lari S Adjuvant and neoadjuvant chemotherapy in osteosarcma 2001(04)

124. Bacci G;Longhi A;Forni C Neoadjuvant chemotherapy for radioinduced osteosarcoma of the extremity:The Rizzoli cxperience in 20 cases 2007(02)

125. Bacci G;Mercuri M;Longhi A Neoadjuvant chemothcrapy for the treatment of ostcosarcoma of the extrcmities:a comparison of results obtained in single-institution and multicenter trials 2004(04)

126. Bacci G;Mercuri M;Ruggieri P Neoadjuvant chemotherapy for malignant fibrous histiocytoma of bone and for osteosarcoma of the limbs:a comparison between the results obtained for 21 and 144 patients,respectively,treated during the same period with the same chemotherapy protocol 1996(02)

127. Bacci G;Picci P;Ferrari S Neoadjuvant chemotherapy for nonmetastatic osteosarcoma of the extremities:the recent experience at the Rizzoli Institute 1993

128. Bacci G;Picci P;Ferrari S Neoadjuvant chemotherapy for the treatment of osteosarcoma of the extremities:excellent response of the primary tumor to preoperative treatment with methotrexate,cisplatin,adriamycin,and ifosfamide.Preliminary results 1995(01)

129. Bacci G;Picci P;Ruggieri P Neoadjuvant chemotherapy for the treatment of osteosareoma of the limhs.Preliminary results in 100 patients treated preoperatively with high doses of methotrexate i.v.followed by cisplatin (i.a.)and adriamycin 1991(01)

130. Cassano WF;Graham-Pole J;Dickson N Etoposide,cyclophosphamide,cisplatin,and doxorubicin as neoadjuvant chemotherapy for osteosarcoma 1991(09)

131. Graham-Pole J;Ayass M;Cassano W Neoadjuvant chemotherapy for patients with osteosarcoma:University of Florida studies 1993

132. Nakano H;Tateishi A;Imamura T Intensive preoperative chemotherapy for osteosarcoma in the lower extremity 1998(4B)

133. Uchida A;Myoui A;Araki N Neoadjuvant chemotherapy for pediatric osteosarcoma patients[外文期刊] 1997(02)

134. Wada T;Isu K;Takeda N A preliminary report of neoadjuvant chemotherapy NSH-7 study in osteosarcoma:preoperative salvage chemotherapy based on clinical tumor response and the use of granulocyte colony-stimulating factor 1996(03)

135. Wynendaele W;van Oosterom AT Neoadjuvant/primary chemotherapy in cancer treatment:what advantage 1999(03)

136. 郭卫;杨荣利;汤小东 成骨肉瘤新辅助化学药物治疗的疗效分析[期刊论文]-中华医学杂志 2004(14)

137. 王臻;黄耀添;黄鲁豫 高危骨肉瘤的临床特点及治疗对策[期刊论文]-第四军医大学学报 2002(05)

138. 牛晓辉;蔡樀伯;张清 ⅡB期肢体骨肉瘤189例综合治疗临床分析[期刊论文]-中华外科杂志 2005(24)

139. Uchida A;Myoui A;Araki N Neoadjuvant chemotherapy for pediatric osteosareoma patients[外文期刊] 1997(02)

140. Wittig JC;Bickels J;Priebat D Osteosarcoma:a multidisciplinary approach to diagnosis and treatment[外文期刊] 2002(06)

141. Bielack S;Jürgens H;Jundt G Pediatric and adolescent osteosarcoma 2010

142. Bacci G;Picci P;Ruggieri P Primary chemotherapy and delayed surgery (neoadjuvant chemotherapy) for osteosarcoma of the extremities.The Istituto Rizzoli Experience in 127 patients treated prcoperatively with intravenous methotrexate (high versus moderate doses) and intraartcrial cisplatin 1990(11)

143. Scully SP;Temple HT;O'Keefe RJ The surgical treatment of patients with osteosarcoma who sustain a pathologic fracture 1996

144. Ferrari S;Palmerini E;Staals EL The treatment of nonmetastatic high gradc osteosarcoma of the extremity:rcview of the Italian Rizzoli expcrience.Impact on the futurc 2009

145. Bacci G;Ferrari S;Longhi A Pattern of relapse in patients with osteosarcoma of the extremities treated with neoadjuvant chemotherapy 2001(01)

146. Dincbas FO;Koca S;Mandel NM The role of preoperative radiotherapy in nonmetastatic high-grade osteosarcoma of the extremities for limb-sparing surgery 2005(03)

147. 牛晓辉 恶性骨肿瘤外科治疗的术前计划及术后评估[期刊论文]-中华外科杂志 2007(10)

148. Lascelles BD;Dernell WS;Correa MT Improved survival associated with postoperative wound infection in dogs treated with limb-salvage surgery for osteosarcoma[外文期刊] 2005(12)

149. Li J;Wang Z;Guo Z Irregular osteotomy in limb salvage for juxta-articular osteosarcoma under computer-assisted navigation 2012(04)

150. Kawaguchi N;Ahmed AR;Matsumoto S The concept of curative margin in surgery for bone and soft tissue sarcoma 2004

151. Fitzhugh CD;Wise B;Baird K Secondary supratentorial primitive neuroectodermal tumor following treatment of childhood osteosarcoma 2009(03)

152. Ferrari S;Bacci G;Picci P Long-term follow-up and postrelapse survival in patients with non-metastatic osteosarcoma of the extremity treated with neoadjuvant chemotherapy 1997(08)

153. Bielack SS;Marina N;Ferrari S Osteosarcoma:the same old drugs or more 2008(18)

154. 孙燕 肿瘤药物治疗百年回顾与展望[期刊论文]-中华肿瘤杂志 2004(11)

155. 孙燕 临床肿瘤50年:创新中发展[期刊论文]-医学研究杂志 2010(04)