Epidemiology of bone and soft-tissue sarcomas

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Abstract

This paper reviews the current literature on the epidemiology of bone and soft-tissue sarcomas and includes the latest World Health Organization classification of these tumours, up-to-date statistics on incidence from the National Cancer Intelligence Network and Public Health England, new advances in genetic predisposition and diagnostic criteria, as well as covering environmental and occupation risk factors.

Keywords classification; epidemiology; risk factors; sarcoma

Introduction

Sarcomas are a rare and diverse group of malignant tumours which arise in connective tissues embryologically derived from the mesenchyme. The mesenchyme develops into the circulatory and lymphatic systems, as well as structural and connective tissues such as muscle, bone, cartilage and fat. Although peripheral nerves originate embryologically from the neural crest, tumours that arise from them are, by convention, grouped with tumours of mesenchymal origin. Sarcomas present a clinical challenge because they are so rare, often resulting in a delay in diagnosis. Best practice guidelines in the UK recommend that they are treated in specialist centres to which suspected cases should be referred under the '2 week rule' according to National Institute for Health and Care Excellence (NICE) criteria.[1]

WHO classification[2]

As part of the International Classification of Diseases (ICD), the World Health Organization (WHO) publishes classification systems for all types of cancer. The 'WHO Classification of Tumours of Soft Tissue and Bone', a sub-classification of ICD, covers sarcomas. This was revised in 2013 and published in a 4th Edition and provides a universal nomenclature, which helps to ensure comparability of international clinical trials and translational research.

Many of the changes from the 3rd Edition have been driven by advances in molecular biology and the rapidly increasing knowledge of the genetics of tumours. As such, the new system of classification includes much more detailed cytogenetic and molecular data. One significant change is the removal of the term, 'malignant fibrous histiocytoma' (MFH). This was previously one of the most common diagnoses within soft-tissue sarcomas, but advances in molecular diagnosis have shown that the majority of these tumours should be classified with other more specific sarcoma types. However, there remains a small number of tumours that do not readily fall under the diagnostic criteria of other specific types. This diagnosis of exclusion is now termed 'undifferentiated pleiomorphic sarcoma'.

There are over 100 morphological subtypes of sarcoma, which for brevity will not be listed in detail here. Instead, this list can be broadly classified as, follows, corresponding to chapters in the WHO classification. More detailed information, can be found on the International Agency for Research on Cancer (IARC) website.

Soft-tissue tumours are broadly categorized into:

- adipocytic tumours
- fibroblastic/myofibroblastic tumours
- fibrohistiocytic tumours
- smooth muscle tumours
- pericytic (perivascular) tumours
- skeletal muscle tumours
- vascular tumour
- chondro-osseous tumours
- gastrointestinal stromal tumours
- nerve sheath tumours
- tumours of uncertain differentiation
- undifferentiated/unclassified sarcomas.

Bone tumours are broadly categorized into:

- chondrogenic tumours
- osteogenic tumours
- fibrogenic tumours
- fibrohistiocytic tumours
- ewing sarcoma
- haematopoietic neoplasms
- osteoclastic giant cell-rich tumours
- notochordal tumours
- vascular tumours
- myogenic, lipogenic and epithelial tumours
- tumours of undefined neoplastic nature.

The incidence of sarcomas

The National Cancer Intelligence Network (NCIN) is a UK-wide partnership operated by Public Health England, which provides a wealth of information about all types of cancer in the UK. The NCIN analyses common national cancer datasets to monitor patterns of care, drive improvement, and support research and audit. Much of the following information has been drawn from NCIN reports, and further information is available at www.ncin.org.uk. Another excellent source of information is the research charity Cancer Research UK and further data are available at www.cancerresearchuk.org.

Sarcomas are extremely rare; soft-tissue sarcomas account for only 1% of malignancies diagnosed in the UK and of those bone sarcomas as a whole are only 0.2% of all diagnosed cancer cases.[3] They have an age-standardized incidence of 45 per million per year as reported from 2010 data. This has increased

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over time from an incidence of 39 per million per year in 1996, although it should be stressed that this increase may simply reflect improved diagnostic techniques rather than a true increase in incidence. In 2010, there were 3298 new cases of soft-tissue sarcoma diagnosed in the UK, of which 51% affected males, and 49% affected females. The yearly incidence of soft-tissue sarcoma is consistently higher in males than females although this difference is rarely statistically significant.[3]

The age-standardized incidence of bone sarcoma has remained fairly constant in the UK since 1996 at around 7.9 per million per year, and the incidence from 2010 was reported by the NCIN as 8.2 per million per year. In 2011, there were 559 new cases of bone sarcoma diagnosed in the UK of which 58% occurred in males and 42% in females, an incidence ratio of more than 13:10. The increased incidence of bone sarcomas in males compared to females is also consistent, but in this case the difference is statistically significant.[3]

The diagnosis, age and site of presenting tumours

Until recently lists of the most common types of soft-tissue sarcoma included malignant fibrous histiocytoma, which has been removed from the WHO classification system. Now the two most common soft-tissue sarcomas in the UK are leiomyosarcoma (22%) and liposarcoma (12%).

The most common site for soft-tissue sarcomas in general is in the extremities (23%) with approximately two thirds of these arising in the lower limbs. In children below the age of 10, the most common site is in the head and neck (23%) with a predominance of rhabdomyosarcoma[4] (Figure 1).

Overall, the incidence of soft-tissue sarcomas increases significantly with age, with more than 65% of cases occurring in patients aged 50 and over. The highest incidence is seen in the over 85 year old age group, particularly males, where the incidence reaches 230 per million per year and exceeds the rate for females of that age by a ratio of 1.9:1. In females, the incidence of soft-tissue sarcomas exceeds that of males between the ages of 45 and 59, due to the preponderance of gynaecological sarcomas in that age group. The incidence of leiomyosarcomas mirrors the increased incidence of sarcomas seen with advancing age, whereas synovial sarcomas are seen more commonly in young adults in their third and fourth decade, and rhabdomyosarcomas predominate in early childhood.[4]

The most common types of bone sarcoma are osteosarcoma, Ewing's sarcoma, chondrosarcoma and chordoma. Overall, bone sarcomas arise most commonly in the lower limbs (38%), with other common areas being the pelvis (16%) and upper limbs (14%). With increasing age the pattern changes, with fewer tumours presenting in the limbs and more being diagnosed in the pelvis. In patients under the age of 20 years, 70% of tumours occur in the extremities, whereas only 40% of bone sarcomas present in the limbs in patients over the age of 40.[5] For further information on the incidence by age of the four most common bone sarcomas see Figure 2, and for more detailed information on the most common sites of presentation, see Figure 3.

Osteosarcomas are most common in childhood, with a peak incidence during the adolescent growth spurt. However, they follow a bimodal distribution, with a second peak in late adult life where they currently occur as late sequelae of radiation exposure or Paget's disease (both covered later).[5]

Ewing's sarcoma is most common in childhood and adolescence, the incidence thereafter tailing off such that it is very uncommon after the age of 30. Proportionally Ewing's sarcoma is the most common bone sarcoma in the under-10 age group, whereas osteosarcoma is proportionally the most common bone sarcoma in the 10–19 year old age group. Ewing's sarcoma has a median age of onset of 15 years.[5]

Chondrosarcoma is the second most common primary bone tumour. It is exceptionally rare in childhood and adolescence and its incidence increases steadily with age. Between the ages of 50 and 59, chondrosarcoma comprises 50% of all primary bone tumours. Although the incidence continues to increase beyond this age, as a proportion of all bone sarcomas its prevalence decreases due to the second peak of osteosarcoma cases in the elderly.[5] Figure 4 shows a chondrosarcoma of the pelvis.

Chordoma, the least common of the four predominant bone sarcomas, arises from remnants of the embryological notochord and thus presents in the axial skeleton. Like chondrosarcoma, it is exceptionally rare in childhood and adolescence, and its incidence increases with age. The overall incidence of chordoma is approximately 1 per million per year.[5]

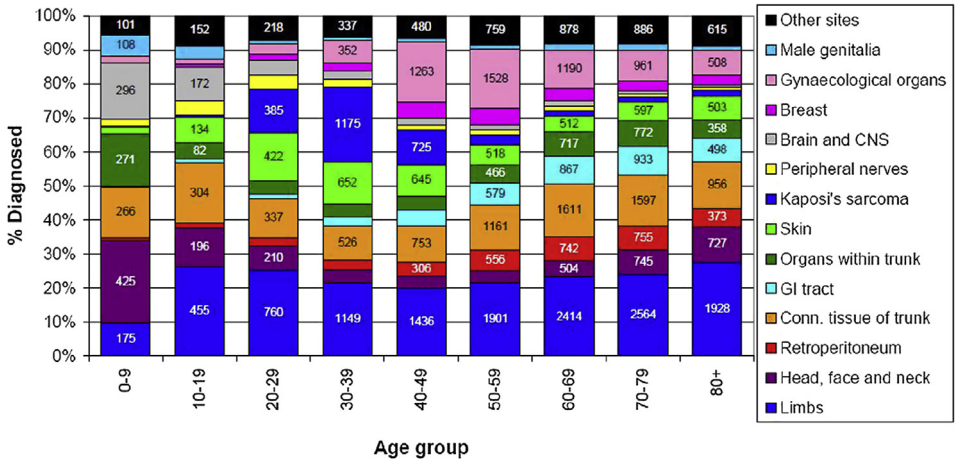

Figure 1 Proportion of soft-tissue sarcomas diagnosed in each age group and anatomical site (England: 1985–2009). Reproduced with permission of Public Health England.[4]

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