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Dwarfism-related skeletal dysplasia in Italy. Multi-analytic study of 8th century CE human remains from Azzio (Varese) and biocultural implications of a pathology

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ABSTRACT

Skeletal dysplasias are a broad family of genetic disorders, often challenging to diagnose even in clinical literature without molecular analysis. Some cases of possible skeletal dysplasia have also been identified in osteoarchaeological samples, although achieving a definitive diagnosis is fraught with difficulties. This paper presents the analysis of the osteological remains of AZ-III-3, discovered in the archaeological context of the Church of Sant'Antonio and Eusebio in Azzio (Varese province, Italy). The study aims to demonstrate that even with limited skeletal elements, a diagnosis can be hypothesised using macroscopic morphometric and radio diagnostic techniques. These methods, compared with clinical and paleopathological literature, have allowed for the identification of a rare Italian case of dwarfism-related skeletal dysplasia. This contribution seeks to address the biocultural presence of individuals affected by these skeletal dysplasias, listing and discussing all published Italian cases, including that of AZ-III-3, whose chronological framework was established through both archaeological context analysis and ^{14}C dating.

1. Introduction

Skeletal dysplasia refers to a group of disorders marked by abnormalities in the development, growth, and maintenance of bone and cartilage (Kinning et al., 2011), classified based on the affected skeletal regions (Handa et al., 2023). In paleopathology, accurate diagnosis is heavily reliant on the preservation of skeletal remains (Assis et al., 2018). Genetic etiology-related skeletal dysplasias are seldom reported in ancient populations, and identifying their specific causes in archaeological specimens is often challenging (Halcrow et al., 2020).

We conduct a differential diagnosis of skeletal dysplasia based on the humerus and femur of AZ-III-3, an 8th century subject from the Italian Alps. We propose a differential diagnosis using macroscopic and radiological analysis. This approach tackles the challenge of working with incomplete remains, which is a common issue in archaeology. Additionally, the study seeks to provide a social and biocultural interpretation of the pathology in Italy by critically reviewing published cases of skeletal dysplasia in the country and incorporating our historical knowledge.

1.1. Archaeological context

The 2012 excavation of the Church of Sant'Antonio and Eusebio (Fig. 1a – GMS N 45°53′8.283″ E 8°42′16.512″) uncovered a multilayered site revealing at least three successive religious buildings with cemeteries dating from the 8th to 13th centuries (Fig. 1b; Grassi et al., 2012). The present church was constructed in 1608 and includes the *putridarium* of the Franciscans, their ossuary (Larentis et al., 2020), and the underground burial chambers of several noble families from the region (Larentis & Calderoni, 2023; Larentis, 2023). Anthropological analyses initially focused on the Franciscan community (Larentis et al., 2023) and the noble families, were eventually extended to the earlier

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layers of the site, pertaining to the cemeteries of the first three churches. The excavation revealed a minimum number of 218 individuals from the 8th to the 19th century (Table 1).

Forty-seven flat graves belong to the cemetery of the first church (Fig. 1 c, 8th-9th century) or of the second church (Fig. 1 d, 9th-13th century). However, the lack of direct stratigraphic relationships between the graves and the uncovered structures, as well as the loss of the burial ground level, prevents a more precise identification of their chronology. Four graves, on the other hand, belong to a cemetery reserved for non-adults, associated with the second church, as the graves align with and follow the layout of the discovered masonry structures.

2. Materials and methods

2.1. Materials

AZ-III-3 comes from the fill of tomb 26, located in the III district of the cemetery associated with the church constructed between the 9th and 13th centuries (Fig. 1c; Table 1). The remains consist of a fragment of right humerus and right femur found within the fill of the pit. The bones, although fragmented, are characterised by excellent preservation of the external cortical surface, allowing for a satisfactory anthropological and palaeopathological evaluation.

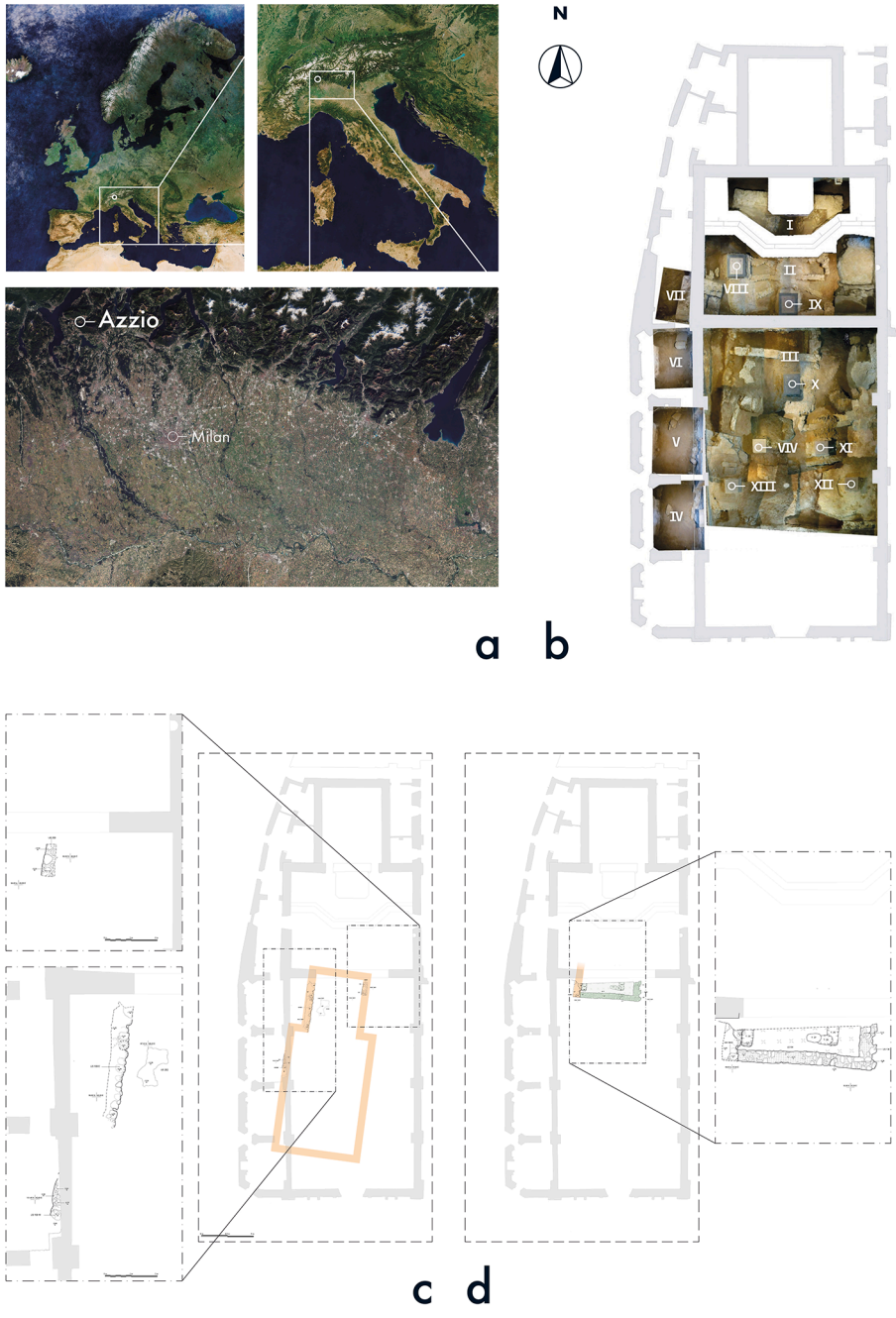

Fig. 1. (a) Location of Azzio. (b) Excavation areas of the Sant'Antonio and Eusebio: I – Presbytery, II – Altar, III – Nave, IV – 1st Chapel, V – 2nd Chapel, VI – 3rd Chapel, VII – Lobby, VIII – Della Porta underground grave, IX – 1st Franciscan Order *putridarium*, X – 1st underground grave, XI – 3rd Franciscan Order underground grave, XII – 2nd underground grave, XIII – De Vincenzi underground grave, 4th underground nave grave). (c) Masonry structures of the first church (8th-9th century) and its hypothetical reconstruction. (d) Masonry structures of the second church with graves 24–27 (9th-13th century).

Table 1
Number of individuals associated with each chronological phase based on archaeological and historical evidence. For further information on the phases and on the archaeological, historical data and the radiocarbon dates used to highlight these phases, see Grassi et al., 2012, Larentis et al., 2020 and Larentis & Calderoni, 2023.

District	Location	8th-13th c	9th-13th c	13th c – 1608	1608 – early 19th c	1704—1740	19th c
I	Presbytery	3	–	–	–	–	–
II	Altar	8	–	3	–	–	–
III	Nave	27	4	16	–	–	–
IV	1st chapel	–	–	–	–	–	–
V	2nd chapel	2	–	–	–	–	–
VI	3rd chapel	5	–	3	–	–	–
VII	Lobby	2	–	3	–	–	–
VIII	Della Porta underground grave	–	–	–	–	3	–
IX	*Putridarium* and ossuary of the 1st Franciscan Order	–	–	–	35	–	1
X	1st underground nave grave	–	–	–	24	–	–
XI	3rd Franciscan Order underground nave grave	–	–	–	24	–	–
XII	2nd underground nave grave	–	–	–	16	–	–
XIII	De Vincenzi underground nave grave	–	–	–	16	–	–
XIV	4th underground nave grave	–	–	–	23	–	–
Total		**47**	**4**	**25**	**138**	**3**	**1**

2.2. Methods

The limited representation and fragmentary nature of AZ-III-3, as well as the absence of an Italian sample from the same area with the same pathology, restricted the use of morphometric comparison techniques for age estimation and sex determination of the subject. However, we compared our sample with both non-adult subjects and adults with skeletal dysplasia to highlight any similarities and to approximate the age (e.g., Garcia & Santos, 2019; Whitmore & Buzon, 2019; Waters-Rist & Hoogland, 2013; Sables, 2010; Frayer et al., 1988). As suggested by other studies (e.g., Debard et al., 2021; Molto & Kilpatrick, 2018; Traversari et al., 2020), we confirm the shorter length of the humerus of AZ-III-3 by comparing it to data on the length of female humeri from the adult population found in Azzio. According to stratigraphic data, these remains date to between the 8th century and 1608. To narrow down the time frame in which the subject died, a 1.24 g fragment of the humeral diaphysis was radiocarbon dated at the University of Milano-Bicocca, with the resulting age calibrated using OxCal 4.4 and the IntCal20 atmospheric curve (Reimer et al., 2020). We have also included the length between the radial fossa and the midpoint of the deltoid tuberosity (RF-DT length) to base our comparison on these measurements. This comparison is necessary because the humerus of AZ-III-3 is broken both distally and proximally. Differential diagnosis was conducted using clinical and paleopathological literature, along with macroscopic and radiological evaluations. The bones were examined using digital radiography and computed tomography, followed by 3D reconstruction (TC system Aquilon Prime model TSX-303°/AC, exposure [100 ms] 55 kV, 100 mA). Each bone fragment was scanned with a 1.0 mm slice thickness and 0.5 mm increments, with images converted to STL format using Mimics software.

3. Results

3.1. Preserved skeletal elements and taphonomy

The humerus is partially preserved, including muscle attachment sites, but is missing the proximal portion and epicondyles, showing clean fractures (Fig. 2a). The femur is less preserved, retaining the lesser trochanter and associated muscle attachments, also displaying light-colored fractures distinct from the patina on the cortical bone (Fig. 2b).

3.2. Radiocarbon dating and age and sex determination

The calibrated radiocarbon date allowed for estimating the death of the individual within the chronological range of 679 to 820 cal CE (Fig. 3). The sex of the subject could not be determined due to the absence of anatomical regions with pronounced sexual dimorphism, the incomplete nature of the evaluated fragments, and the lack of elements within these fragments that could potentially suggest skeletal sex. The robustness of the diaphyses and the clearly visible enthesopathies suggest that the subject had reached, or was close to reaching, full skeletal development, allowing us to estimate a skeletal age of over 20 years.

3.3. Morphological macroscopic analyses

Bones exhibit severe alterations in the normal anatomical harmony that should distinguish them (Fig. 2). A posterior bowing of the distal humerus is also evident, determined by lines drawn parallel to the mid-diaphyseal and distal diaphyseal axes (Fig. 4 a). The insertion of the humerus at the deltoid tuberosity is particularly pronounced (Fig. 4 b), as is the general prominence of the other muscle attachments (Fig. 4 c). Additionally, the diaphysis at the level of the deltoid tuberosity begins to angle dorsally. Within the olecranon fossa, an ellipsoidal apposition of cortical-like bone advancing towards the trochlea is visible, without involving the articular area (Fig. 4 d). The femur is similarly characterised by particularly prominent muscle attachment areas in the posterior part of the diaphysis (Fig. 5a). The appearance of the greater trochanter deviates from the expected morphology; it is flat and features a porous endophytic surface where the psoas major muscle attaches (Fig. 5b). In the lateral view, the attachment of the *gluteus maximus* and the origin of the *vastus medialis* are evident (Fig. 5c).

3.4. Metric evaluation

The humerus fragment measures 13.6 cm in length, and the distance between the radial fossa (RF) and the deltoid tuberosity (DT) is 9.7 cm. On average, the humeri of adult females buried in the cemeteries at the Azzio site have a total length of 26.2 cm, and the average distance between their RF and DT is 12.8 cm (Table 2).

3.5. Radiological evaluation

The radiological analysis enabled the construction of 3D models of the bone fragments (Figg. 6–7), which are particularly useful for preserving the shape of the humerus before sampling for ^{14}C analysis. The cross-section of the humeral diaphysis shows that the cortical bone of the deltoid tuberosity is very thin, while the interior contains sparse spongy bone (Fig. 6 a). This section also highlights the anomalous angulation of the shaft at this height. Additionally, CT radiographic acquisitions provided data on what appeared morphologically to be an ellipsoidal apposition of bone tissue in the upper part of the olecranon fossa (Fig. 6 b, d). It is a bone button characterised by fine trabeculae inside, connected to the humerus by a thin layer of cortical bone (Fig. 6 c), making it difficult to recognize a well-defined perimeter also on the

Fig. 2. Right humerus (a) and right femur (b) of AZ-III-3. For both bones, from left to right, the postero-anterior, lateral, antero-posterior, and medial views.

outer surface. It is also possible to see how the bony protuberance is composed of at least two bone fragments (Fig. 6 d).

The transverse section at the greater trochanter of the femur reveals an area of lower bone tissue density at the insertion of the *iliopsoas* (Fig. 7 a), with its surface featuring a thin layer of hypodense cortical bone (Fig. 7 b). The origin of the *vastus medialis* is characterised by a very thin layer of cortical bone, immediately beneath which lies fine trabecular bone tissue (Fig. 7 c), while at the insertion of the *gluteus maximus* there is an area of heterotopic ossification (Fig. 7 d). A lower transverse section of the diaphysis shows how the trabecular bone tissue affects the development of the *vastus medialis* in the diaphysis (Fig. 7 e).

4. Discussion

4.1. Taphonomy, chronology and biological profile of AZ-III-3

The fractures in the bones are likely recent and occurred post-mortem, possibly during careless retrieval, as indicated by the lack of patina and sharp edges (Johnson et al., 2016). Despite this, the well-preserved external surfaces allow for accurate palaeopathological analysis.

The radiocarbon calibrated date on the human bone fragment of AZ-III-3 is consistent with the stratigraphic data, indicating the construction of a new church beginning in the 9th century. Consequently, the old-wood effect in the radiocarbon date is unlikely or negligible (Ramsey, 2009). The burial of AZ-III-3 was likely disturbed by the construction of the second church or intercepted during the excavation of the pit that contained the subject of tomb 26, ending up in its fill. The discovery of

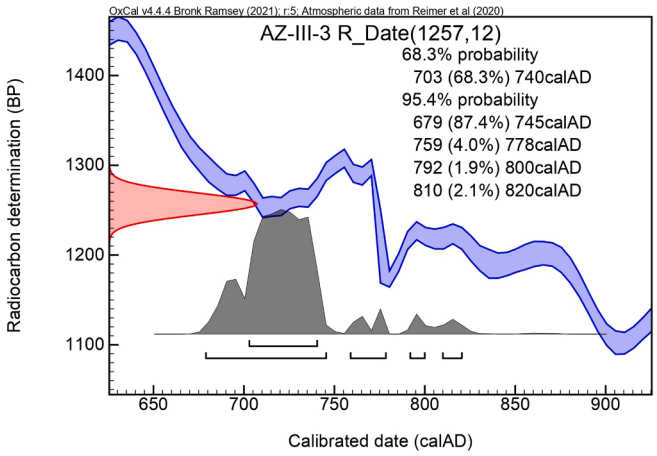

Fig. 3. OxCal plot showing the uncalibrated and calibrated radiocarbon date of a fragment of human humerus diaphysis of AZ-III-3 from Azzio (Varese, Italy).

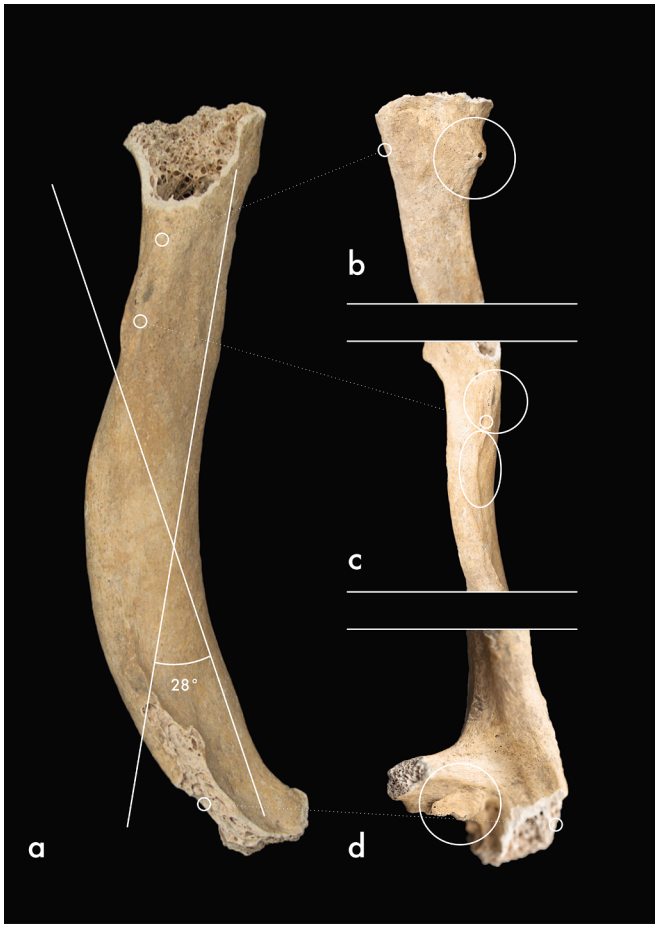

Fig. 4. (a) Lateral view of AZ-III-3 humerus, the lines drawn are parallel to the mid-diaphyseal and distal diaphyseal axes and form an angle of 28°; (b) Pronounced insertion of the deltoid tuberosity and the thinness of the cortical bone, which is fractured at one point exposing the trabecula; (c) Detail of the prominent origin of the medial head of the triceps brachii (top) and the pronounced insertion of the coracobrachialis muscle (bottom); (d) Bone apposition within the olecranon fossa.

bone fragments from other individuals within the fill of tombs is a well-known phenomenon, especially in cemeteries of multi-layered sites like Azzio (Cherstich et al., 2018). In the absence of aDNA testing, it is not possible to definitively state that the bones attributed to AZ-III-3 belong

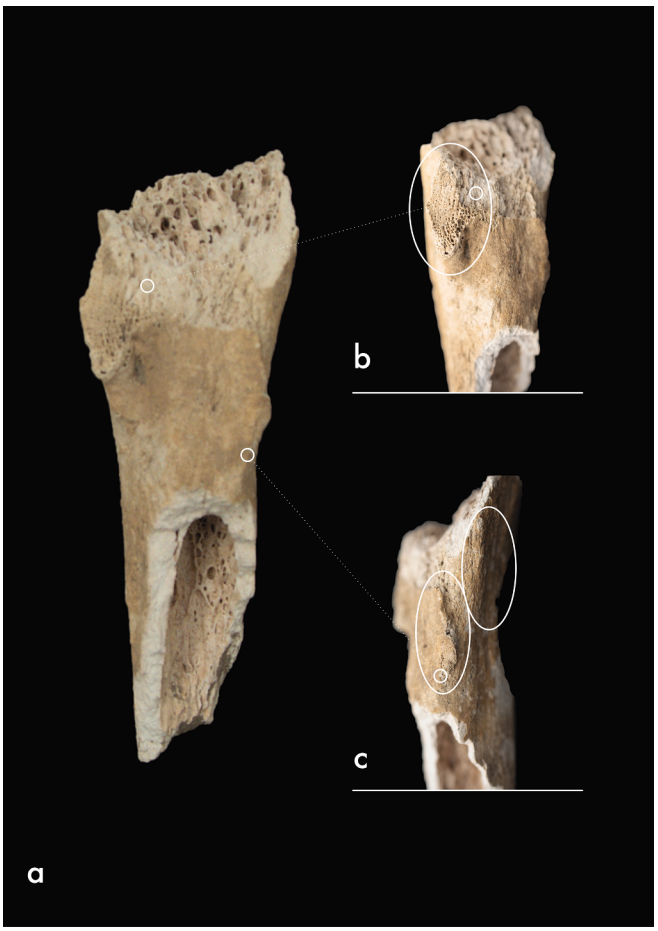

Fig. 5. (a) Posterior view of AZ-III-3 femur: (b) the greater trochanter is flattened and the surface is characterised by a layer of remodelled bone tissue, with sparse pitting in the lower portion; (c) the muscle attachment of gluteus maximus (bottom) and of the vastus medialis (top) areas in the proximal portion of the diaphysis are particularly pronounced.

to a single individual, given the difficulty in determining sex and age from the bones (Maixner et al., 2021). However, considering the incidence of skeletal dysplasias, among which achondroplasia is one of the most common short-limb dwarfism pathologies with an incidence of approximately 1:20,000 to 1:30,000 live births per year (Waller et al., 2008), and the population of Azzio, estimated at around 400–450 inhabitants during the pre-Jennerian period (ISTAT, 1960), it seems unlikely that two individuals with this pathology would be found in the same archaeological phase.

Age estimation is challenging, but the well-defined insertion areas on the humerus and femur suggest pronounced heterotopic ossification, typical in dwarfism-related skeletal dysplasia, less evident in developing skeletons (e.g., Garcia & Santos, 2019; Whitmore & Buzon, 2019; Waters-Rist & Hoogland, 2013; Sables, 2010; Frayer et al., 1988), allowing us to hypothesize an adult age for AZ-III-3. Regarding the sex of the subject, no morphometric criteria could be applied, and the lack of comparative individuals with the same pathology from the same geographical area did not allow for the parameterization of a metric method for sex determination for AZ-III-3.

The bone fragments exhibit unusual morphological traits, likely linked to dwarfism-related skeletal dysplasia. Despite the limited fragments, accurate differential diagnosis was possible because the femur and humerus are key elements for assessing such conditions. (Halcrow et al., 2020; Debard et al., 2021; Matczak et al., 2022).

Table 2
Total length and Radial fossa – deltoid tuberosity length values acquired from the adult female sample from Azzio, dating between the 8th century and 1608, and from AZ-III-3.

ID	Cronology	Total lenght	RF-DT lenght
AZ-III-3	8th-13th c	–	9.7
AZ-I-2	8th-13th c	27.3	12.3
AZ-II-3	8th-13th c	26.3	12.8
AZ-II-4	8th-13th c	–	13.1
AZ-II-6	8th-13th c	25.3	12.4
AZ-II-9	13th c – 1608	23.9	11.9
AZ-III-2	8th-13th c	24.5	11.8
AZ-III-4	8th-13th c	–	12.7
AZ-III-5	8th-13th c	–	12.3
AZ-III-6	8th-13th c	27.2	13.5
AZ-III-11	8th-13th c	26.8	13.2
AZ-III-12	8th-13th c	24.2	12.5
AZ-III-17	8th-13th c	–	13.2
AZ-III-18	8th-13th c	25.3	12.6
AZ-III-20	8th-13th c	26.0	12.9
AZ-III-23	8th-13th c	27.3	13.5
AZ-III-24	8th-13th c	–	11.9
AZ-III-26	8th-13th c	27.4	13.1
AZ-III-32	13th c CE – 1608	26.9	13.3
AZ-III-33	13th c CE – 1608	26.2	12.9
AZ-III-37	13th c CE – 1608	26.4	12.7
AZ-III-42	13th c CE – 1608	25.7	12.6
AZ-V-2	8th-13th c	–	12.3
AZ-VI-3	8th-13th c	27.1	13.1
AZ-VI-5	8th-13th c	25.8	12.8
AZ-VI-6	13th c – 1608	–	13.2
AZ-VII-4	13th c – 1608	27.5	13.7

4.2. *Differential diagnosis*

The analysis began by comparing the humeral diaphysis lengths of AZ-III-3 with those of normal adult females from the Azzio sample. This involved measuring and comparing both the total lengths and RF-TD lengths of the humeri. (Table 2). The RF-TD values of adult females average 12.8 cm with a standard deviation of 0.50, assuming a Gaussian distribution. Comparing the RF-TD value of AZ-III-3, the deviation from the average value is about 6 standard deviations. Therefore, it can be excluded with high confidence that the subject AZ-III-3 belongs to the same statistical population (e.g., Molto & Kilpatrick, 2018). The metric analysis, supported by macroscopic anthropological evaluations, confirmed the reduced length of the subject's humerus.

Subsequently, we sought to gather information on whether the humerus was affected by rhizomelia, a condition characterized by the shortening or deformity of the proximal limb segments (Rayan & Upton III, 2014). The cross-section of the humerus at the level of the deltoid tuberosity shows an abnormal angulation due to the flattening of the posterior cortical wall and the compression of the anterior one (Fig. 6a). This specific morphology of the diaphysis is observed in paleopathological cases of upper limb rhizomelia (e.g., Hoffman, 1976; Frayer et al., 1987, 1988; Waters-Rist & Hoogland, 2013; Slon et al., 2013) and is absent or significantly mitigated in non-rhizomelic skeletal dysplasias (e.g., Arcini & Frölund, 1996; Milella et al., 2015). Therefore, the morphological analysis and comparison with the literature suggest that the humerus of AZ-III-3 was affected by rhizomelia.

A notable feature in the assessment of the humerus is the anterior curvature of the distal diaphysis (Fig. 2a). This curvature can be quantified with an angle obtained by intersecting two lines parallel to the mid-diaphyseal and distal diaphyseal axes. In our case, the resulting angle is 28°, and the clinical literature reports that above 20°, the elbow fails to fully extend, while slightly above 28°, there is total loss of extension (Bailey, 1971; Kitoh et al., 2002). The almost complete loss of elbow extension in AZ-III-3 might have increased the incidence of trauma to the area, and the elliptical apposition on the humerus (Fig. 6 b-d) could be interpreted as a fragment of the ulna fused there following

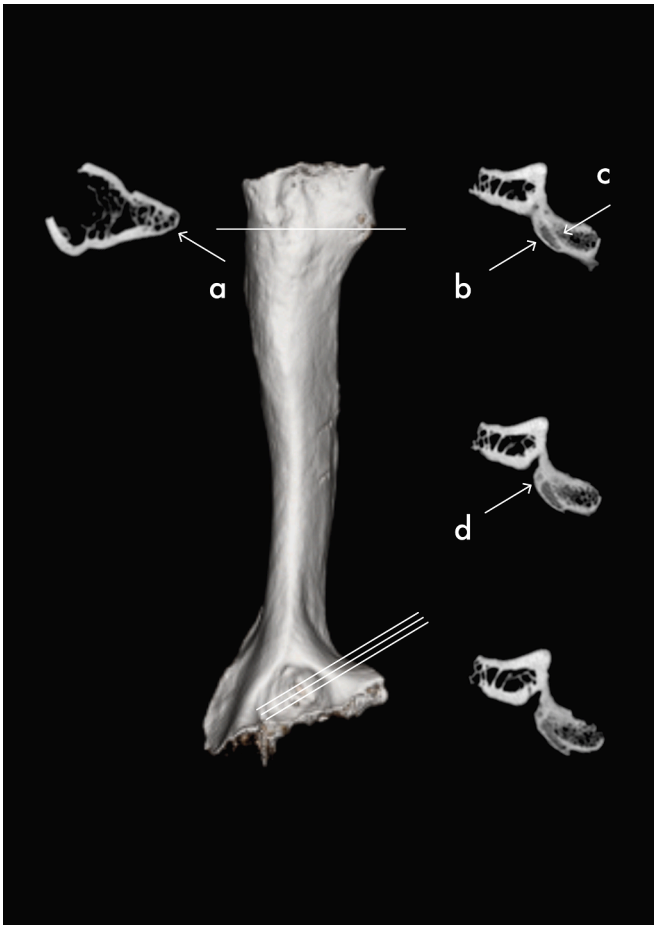

Fig. 6. 3D model of the right humerus of AZ-III-3. (a) Transversal section of the diaphysis at the level of the deltoid tuberosity, characterised by a very thin layer of cortical bone and dense trabecular bone. Oblique transverse sections of the upper portion of the olecranon fossa highlight the trabecular structure of the bony protuberance (b), separated by a thin layer of cortical bone from the medial portion of the fossa (c). (d) This protuberance is composed of at least two fragments.

an olecranon fracture (Appelboam et al., 2008; Wiegand & Bernstein, 2012; Sullivan & Desai, 2019). This type of fracture accounts for 10 % of those affecting the upper limbs, with an incidence of 12:10,000 (Connor et al., 2023) and a mean age of occurrence of 57 years. It is also not possible to rule out that it may be the result of osteoarthritic phenomena, although in such cases, the bone plate should not exhibit trabecular tissue (Martinez-Catalan et al., 2021). However, this remains speculative as the absence of the ulna precludes further data acquisition to verify this hypothesis.

The humerus, like the femur, shows heterotopic ossification in the muscle insertion and origin areas. Pronounced enthesopathies are a widespread characteristic in skeletal dysplasias, particularly those involving rhizomelic appendicular involvement (e.g., Matczak et al., 2022; Whitmore & Buzon, 2019; Cormier et al., 2017; Nater et al., 2016). Additionally, the greater trochanter, where the iliopsoas insertion is flat and characterized by dense and porous cortical tissue, stands out. In cases of skeletal dysplasia, femoral modifications are well-documented, as is the involvement of the vastus medialis and iliopsoas, a deep muscle crucial for mobility that directly connects the femur to the spine (e.g., Ando et al., 2021; Debard et al., 2021; Traversari et al., 2020; Cormier et al., 2017; Nater et al., 2016).

Specifically, the radiological appearance of the cross-section of the deltoid tuberosity and the vastus medialis insertion both exhibit a very thin cortical layer immediately followed by mature and dense trabecular

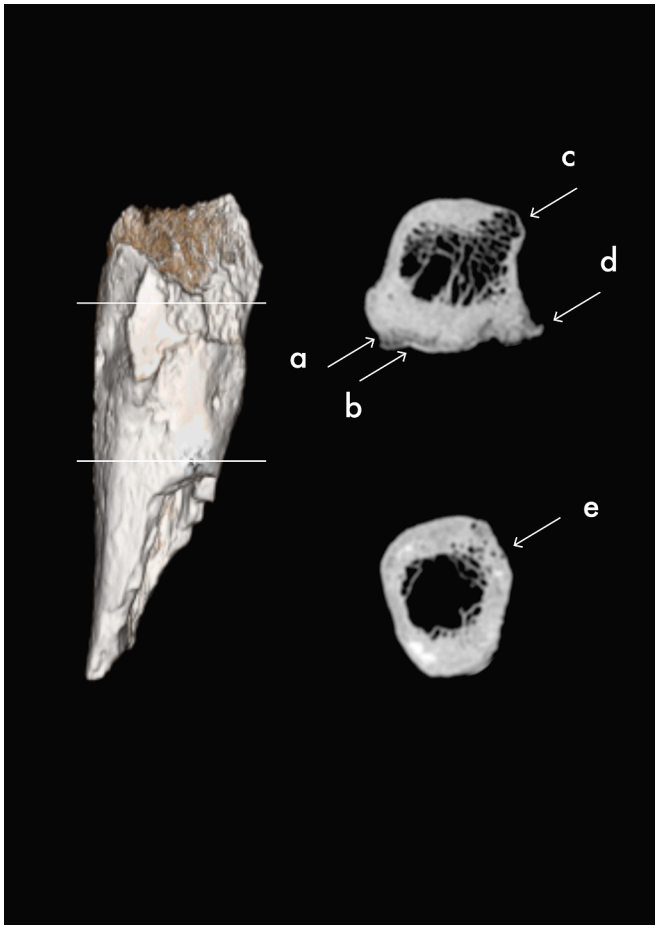

Fig. 7. 3D model of the right humerus of AZ-III-3. (a) Hypodensity of the cortical bone at the level of the third trochanter. (b) Thin layer of dense bone at the insertion of the iliopsoas; (c) Very thin cortical bone tissue with a large area of trabecular bone beneath (d). (e) Trabecular bone tissue is also observed in a lower portion of the diaphysis in conjunction with the vastus medialis.

tissue towards the medullary cavity; these features align with dwarf-related skeletal dysplasia in both paleopathological and clinical data (e.g., Woo et al., 2015). Given the previous considerations, our differential diagnosis considered the main pathologies affecting the humerus and femur (Table 3). Considering the data obtained, the pathological and morphometric evidence of AZ-III-3 seems to align more closely with clinical and paleopathological findings related to achondroplasia. However, given the limited representation of the femur and the absence of most of the skeleton, it is not possible to entirely rule out Chondrodysplasia punctata and especially Pseudoachondroplasia beyond a reasonable doubt. These last two pathologies were chosen as they are more illustrative of morphological changes in bones that are easily detectable in osteoarchaeological samples. However, we want to emphasize that a differential diagnosis within the broad family of dwarfism-related skeletal dysplasia is extremely complex in the absence of molecular analyses (Scocchia et al., 2021).

Table 3
Differential diagnosis of the skeletal evidence of AZ-III-3 from a) Debard et al., 2021; b) Traversari et al., 2020; c) Matczak et al., 2022; d) Kitoh et al., 2002; e) Pauli, 2019; f) Cormier et al., 2017; g) Woo et al., 2015. ACH = Achondroplasia, CDP = Chondrodysplasia punctata, MED = Multiple epiphyseal dysplasia, MPS = Mucopolysaccharidosis, PSACH = Pseudoachondroplasia.

Skeletal evidence	ACH	CDP	MED	MPS	PSACH	AZ-III-3
Humeral rizhomelia[c,f]	X	X	–		X	X
Irreguar humeral epypheses[a, b,c,f]	X	X	X	X	X	X
Humeral hypertrophies at muscular attachment [b, c]	X	X	X	–	X	X
Angle of posterior bowing of distal humerus > 20°[c, d, e,]	X	–	–	–	–	X
Irregular femoral epypheses[a, b,c,f]	X	X	X	X	X	X
Femoral hypertrophies at muscular attachment [b,c]	X	–	X	–	X	X
Greater trochanter modifications[a, b, c,]	X	–	X	–	X	X

4.3. Clinic features of achondroplasia

Achondroplasia (OMIM: 100800; ORPHA: 15) is a rare genetic disorder that affects bone growth in the limbs, resulting in short stature. This condition falls under skeletal dysplasias, a group of disorders impacting bone and cartilage development (Elfina & Ramadhani, 2019). The disorder stems from a mutation in the FGFR3 gene, which is crucial for normal bone growth and development, as it produces the fibroblast growth factor receptor 3 protein (Chaudhry et al., 2021). Achondroplasia is the most common form of disproportionate short stature, with an incidence rate of about 1 in every 20,000 to 30,000 people. This translates to an estimated global population of 250,000 individuals affected by the condition (Ireland et al., 2014). The disorder follows an autosomal dominant inheritance pattern, meaning that inheriting the mutated FGFR3 gene from just one parent is sufficient to develop the disorder.

The clinical features of achondroplasia are apparent at birth. These include a large head (macrocephaly), prominent forehead (frontal bossing), flattened nasal bridge, underdevelopment of the midline facial region (midline facial hypoplasia), and short, stubby limbs (rhizomelia). The hands are typically short and broad, often showing a trident configuration. Additionally, individuals may have a small opening in the base of the skull (hypoplastic foramen magnum) and a small skull base (Simmons et al., 2014; Waller et al., 2008). People with achondroplasia face an increased risk of several health complications. These can include recurrent ear infections, sleep apnea, and spinal stenosis (Rimoin, 2013). There is also a higher incidence of obesity, which can worsen these health issues. Despite these challenges, most individuals with achondroplasia have normal cognitive development (Rimoin, 2013).

4.4. Skeletal dysplasia in Italian archaeological contexts in Italy

Upon identifying the potential pathology in the subject as achondroplasia or another dwarf-related skeletal dysplasia, we questioned how such a disease, which could lead to evident physical deformities, motor difficulties, and sometimes cognitive impairments (Lachman, 1997), was perceived by society and the relationship between society and affected individuals. To answer this question, we conducted a targeted bibliographic survey to find cases of skeletal dysplasia in Italian archaeological contexts.

Our analysis reveals a sparse literature, with five cases ranging from the late Epigravettian to the late Middle Ages. Chronologically examining these findings, we begin with the first known case in the literature of dwarfism-related skeletal dysplasia, identified as an individual with acromesomelic dysplasia (Frayer et al., 1987, 1988; Tilley, 2015). This was a non-adult individual, aged 17–20, probably male, from a hunter-gatherer group in southern Italy. Much has been discussed about the human group's role in the care of Romito 2. Among the various theories, the most convincing is that proposed by Tilley, who, through the application of bioarchaeology of care theories and the use of the Index of Care, confirms the interpretation of Frayer and colleagues. According to Tilley, this hunter-gatherer community provided communal care for individuals with health-related disabilities; even after death, the individual remained part of the community, sharing the same burial places and rituals.

Another significant case is that of a 20–25-year-old individual found in Via Serenissima, in the excavation that unearthed more than 2200 burials of the Imperial necropolis of Collatina in Rome (Minozzi et al., 2013). The burial was in a marginal area of the necropolis, without any grave goods or clothing, with the individual in a left lateral position, an unusual position, and with the head inserted into an amphora. Given these variables, it has been hypothesised that the individual belonged to a very humble social class. However, it remains to be understood whether the marginalisation within the necropolis and at a ritual level is related to social status or the society's perception of the disease. For this finding, we highlight some evidence, proposing a new interpretation. The amphora in which the head is inserted is a Gauloise 4 wine amphora from France, widely distributed from the Mediterranean basin to Britain, dated from the Julio-Claudian era to the 3rd century (Pannella, 2001). The presence of a dwarf in a marginal area of the cemetery, without grave goods, in an anomalous position, and with the head hidden in an amphora, appears to be unique in the context of Italian burials from the 1st-3rd century. It is plausible to question whether this burial can be seen in a context where dwarfs were part of the elite entourage or, as we propose, this burial reflects a new social status and perception of dwarfs in Roman society following the laws enacted by Alexander Severus in the first half of the 3rd century.

In the case of tomb 17 from Piazza XX Settembre in Modena, the individual was part of a large privileged burial cluster in an important city cemetery, that of Piazza Grande (Traversari et al., 2020). The individual in tomb 17 had a rich array of grave goods, even compared to other tombs. The study of the objects identifies the subject as a young first-generation Lombard, granted all privileges in terms of grave goods and clothing items, including the right to be buried within a prestigious context. From this case, it can be hypothesised that the Lombards reserved the same rights and rituals for individuals with skeletal dysplasia, to the extent that one of them had arrived in Italy during the first migratory waves and was buried with all honours according to their tradition.

The find at Pieve Pava concerns an 18–20-year-old male buried with regard within the church in the second half of the 7th century (Ricci et al., 2012). More controversial is an adult male from the 11th-15th century in Cividale del Friuli, buried prone in a double grave, accompanied by a female skeleton (Baggieri et al., 2003). This burial has been interpreted as an anomalous context, where the individual was placed in a non-conforming manner to the ritual, perhaps due to his pathology.

For AZ-III-3, the available information is scarce, allowing only the hypothesis that his body lay in consecrated ground, alongside other individuals sharing the cemetery space of the first church of Azzio between the 8th and 9th centuries.

4.5. The perception of skeletal displasya in the past Italy

To better contextualise the Italian archaeological finds from the historical period onwards, we analysed the available sources and information. During the Regal and Republican ages (753–31 BCE), individuals with physical imperfections could be drastically eliminated, as noted in the Twelve Tables (Table IV, 1). In the Imperial age, their fate improved, and dwarfs were often considered companions or advisors to the elite (Maiuri, 2012; Pliny the Elder, Naturalis Historia, 7.75–76; Suetonius, Augustus, 43.3) or curiosities to be shown to guests (Trentin, 2011). There are records of adult individuals following matrons according to Greek-Ionian custom (Martial, Epigrammaton, XCIII) and accompanying emperors such as Tiberius (reigned: 14–37 CE) (Suetonius, Tiberius, LXI) and Domitian (reigned: 81–96 CE) (Suetonius, Domitian, IV). We know from the same sour that Domitian celebrated Saturnalia with fights between women and dwarfs, the only beings who, due to their physique, could challenge women. The search for dwarfs was so intense that there are accounts of the practice of confining children in special boxes to constrain their growth, making them disharmonious and thus increasing their economic value (Seneca, Controversiae, X,4; Longinus, Del Sublime, 44,5). From the emperor Alexander Severus (reigned: 222–235 CE) onwards, a policy against the use of dwarfs began, freeing dwarfs and dwarf women performing at court, suggesting this practice was widespread (Historia Augusta, Alexander Severus, 34.2–4). With Severus, a change in attitude towards dwarfs began, further accentuated by Christian doctrine and the semantic shift in the concept of diversity. Augustinian teachings state that *"Honor enim hominis verus est imago et similitudo dei […]"* (Augustine, De Trinitate, XII,11,16) ("The true honour of man is the image and likeness of God"), implying that deviation from God's image represents a different type of representation of the divine concept. Physical diversity was now associated with moral deviation from God and thus the loss of all social value. Theoretically, in the Middle Ages, pathology was seen as an expiation of guilt (Umberto da Romans, De Eruditione Predicatorum II,XCII), in a dichotomy that on one hand imposed the obligation of charity towards the weak and on the other considered disease as punishment or expiation of sins. Thus, dwarfs, along with Muslims, Jews, hermits, prostitutes, lunatics, prisoners, and lepers, became part of the society of the excluded, without the right to burial in consecrated ground. These individuals were considered outlaws and subject to popular justice (Thomas Aquinas, Summa Theologica, 2.2.quaest.168 art.3). Only after the Council of Ravenna in 1286 was condemnation directed solely at street dwarfs, acrobats, and freaks who were part of the marginalised. As is well known, the figure of the dwarf as a companion, jester, and advisor returned to prominence in the Italian Renaissance, with well-known stories and figures in literature.

5. Conclusions

Based on the anthropological and paleopathological analysis, the study has identified a case of dwarf-related skeletal dysplasia, most likely achondroplasia, through a differential diagnosis of a skeleton with only a few recovered elements. Despite the challenges posed by the incomplete nature of the skeleton, the study demonstrates that even limited yet significant elements can guide a thorough differential analysis.

The subject, AZ-III-3, of undetermined sex and at least adult age, was estimated to have died between 679 and 820. This chronological framework, established through both archaeological context analysis and ^{14}C dating, allows for meaningful comparisons with other known medieval cases. During the Middle Ages, the treatment of individuals with dwarfism varied widely, often depending on the cultural and social context. Dwarfs were sometimes regarded with a mixture of curiosity and reverence and were often employed as court jesters or entertainers, where their stature and perceived eccentricities were exploited for amusement. However, they could also be seen as objects of wonder or as possessing special qualities.

Burial practices for dwarfs during this period reflected these varied perceptions. In some cases, they were buried in regular cemeteries alongside other individuals, indicating their integration into the community. In other instances, their burials might reflect their status in life, whether as cherished members of noble households or as marginalized individuals. The specific archaeological evidence from the church of Saints Anthony and Eusebius in Azzio indicates that dwarfism was present in medieval populations and that individuals with this condition were interred in communal burial grounds without distinct differentiation from other members of the community. This study also highlights the importance of considering both the biological and cultural contexts in the analysis of skeletal remains, providing a more comprehensive understanding of the lives and treatments of individuals with skeletal dysplasia in historical populations.

CRediT authorship contribution statement

Omar Larentis: Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Investigation, Formal analysis,

Data curation, Conceptualization. **Enrica Tonina:** Formal analysis. **Massimo Venturini:** Supervision, Formal analysis. **Ilaria Gorini:** Writing – review & editing, Supervision, Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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