The accuracy of different imaging techniques in diagnosis of acute hematogenous osteomyelitis

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***Key words**: acute hematogenous osteomyelitis; diagnostic accuracy; sensitivity; specificity; diagnostic odds ratio.*

***Summary.** Objective. The aim of this study was to establish and compare diagnostic accuracy (sensitivity, specificity, and diagnostic odds ratio) of plain x-ray, ultrasonography, bone scintigraphy, computed tomography (CT), and magnetic resonance imaging (MRI) in pediatric acute hematogenous osteomyelitis.*

Material and methods. Analysis of patients' data, hospitalized at the Department of Pediatric Surgery with suspected acute hematogenous osteomyelitis in the period of 2002–2008, was carried out prospectively. Inclusion criteria were age of 1–18 years, pain in bone area, fever, functional disorder, and (or) signs of infection. Plain x-ray, ultrasonography, bone scintigraphy, computed tomography, and magnetic resonance imaging were performed. The recommendations of Standards for Reporting of Diagnostic Accuracy were used in study design.

Results. A total of 183 patients were included into the study. Acute hematogenous osteomyelitis was diagnosed in 156 (85%) patients, and 27 (15%) had other diseases. A total of 169 early plain x-rays (median on the first day of hospital stay), 142 late x-rays (15th day of hospital stay), 82 ultrasonographies (second day), 76 bone scintigraphy (third day), 38 MRI scans (seventh day), and 17 CT (15th day) were performed. The sensitivity of ultrasonography was 0.55 (95% CI, 0.43–0.67); specificity, 0.47 (95% CI, 0.24–0.7); and diagnostic odds ratio, 1.08 (95% CI, 0.3–3.84). The sensitivity of CT was 0.67 (95% CI, 0.38–0.88); specificity, 0.5 (95% CI, 0.01–0.98); and diagnostic odds ratio, 2.0 (95% CI, 0.02–172.4). The sensitivity of early x-ray was 0.16 (95% CI 0.1–0.23); specificity, 0.96 (95% CI, 0.78–1.0); and diagnostic odds ratio, 4.34 (95% CI, 0.63–186.3). The sensitivity of MRI was 0.81 (95% CI, 0.64–0.93); specificity, 0.67 (95% CI, 0.22–0.96); and diagnostic odds ratio, 8.67 (95% CI, 0.91–108.5). The sensitivity of late x-ray was 0.82 (95% CI, 0.75–0.88); specificity, 0.92 (95% CI, 0.62–1.0); and diagnostic odds ratio, 51.17 (95% CI, 6.61–2222.0). The sensitivity of bone scintigraphy was 0.81 (95% CI, 0.68–0.90); specificity, 0.84 (95% CI, 0.60–0.97); and diagnostic odds ratio, 22.30 (95% CI, 4.9–132.7).

Conclusions. Our analysis showed that late x-ray is the most valuable radiologic method in the diagnosis of acute hematogenous osteomyelitis, but bone scintigraphy and magnetic resonance imaging are the most valuable tests at the onset of the disease.

Introduction

Acute hematogenous osteomyelitis (AHO) in children is a serious pediatric disease; its diagnosis sometimes is difficult, and the treatment is long lasting.

Medical progress and environmental changes had an impact on classical symptoms and course of pediatric osteomyelitis (1–3). Fulminate and chronic forms of osteomyelitis are less common than a few decades ago. Physicians see children with AHO earlier; the symptoms are not so obvious because of the initiated treatment with antibiotics, and more patients have subacute forms of AHO. Subacute osteomyelitis is characterized by mild complaints and clinical symptoms, which can continue weeks until correct diagnosis (4–7). Acute osteomyelitis is successfully treated conservatively with antibiotics. The isolation of microbic agent, found in the focus of the disease, is the most important test confirming the diagnosis of AHO. However, this test is of limited value in conservatively treated patients. That is why different

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noninvasive radiologic techniques are becoming more and more important in the diagnosis of AHO. Plain x-ray, bone scintigraphy with radionuclide agent, ultrasound, magnetic resonance imaging (MRI), and computed tomography (CT) can complement each other in the diagnosis of osteomyelitis. It is important to know advantages and disadvantages of each technique and its accuracy and diagnostic value in the diagnosis of children's acute hematogenous osteomyelitis. No studies on the accuracy of bone scintigraphy, CT, MRI in the diagnosis of AHO have been performed in Lithuania. Two decades ago, one study was carried out to test the diagnostic value of ultrasonography in AHO (8). The aim of the present study was to evaluate and compare diagnostic accuracy of plain x-ray, ultrasonography, bone scintigraphy, CT, and MRI in the diagnosis of pediatric AHO.

Patients and methods

Methodology and study design were chosen according to the recommendations of Standards for Reporting of Diagnostic Accuracy (STARD) (9).

During the period of 2002–2008, 1–18-year-old patients with suspected AHO, admitted to the Department of Pediatric Surgery, Hospital of Kaunas University of Medicine, were included in the prospective study. Inclusion criteria were pain on palpation of bone or joint, functional disorder, fever, or (and) other signs of local or general infection. Plain x-ray, ultrasound examination, bone scintigraphy with Tc99, CT, and MRI were performed according to the clinical indications. Bone scintigraphy was performed using a 3-phase bone scintigraphy protocol, with 99m-Tc marked sodium medronate (Amerscan Medronate II Agent, GE Healthcare) with a Siemens E-CAM gamma 2-detector chamber. The dose of radiopharmaceutical agent was calculated according to the recommendations of the Pediatric Task Group of European Association of Nuclear Medicine (EANM). MRI was performed with a 1-tesla Philips Gyroscan T10NT scanner, in T1 and T2 regimens. CT was done using a helical Siemens CT scanner. Ultrasonography was performed with 3 multi-frequent transducers (2 to 14 MHz). The exact frequency was chosen according the density and depth of tissues.

The simplified scheme of radiologic examination is shown in Fig. 1. We performed plain x-rays two times: early x-rays just after hospitalization and late

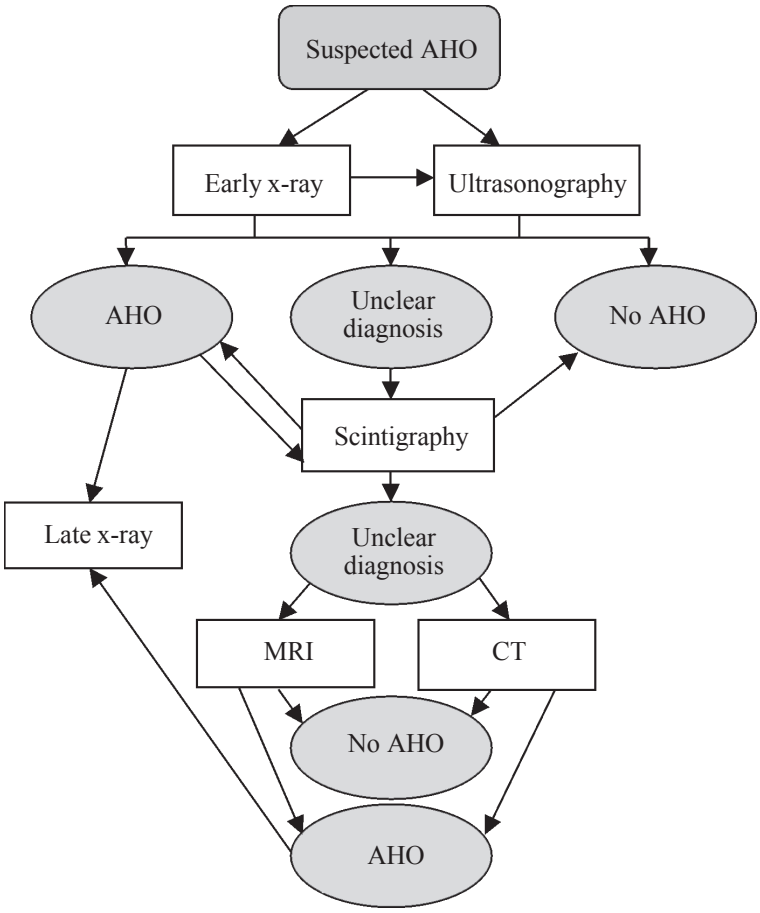

Fig. 1. **The scheme of radiologic investigation**

x-rays not earlier than after two weeks from the onset of the disease. According to the final diagnosis, the results were classified as true positive and negative, false positive and negative. The diagnosis of AHO was made based on typical clinical symptoms (local pain, fever) and (or) laboratory signs of bacterial infection and anyone of these symptoms: positive blood culture, positive culture from the bone, inflammation in the smears from bone, pus found in bone during operation and radiologic confirmation. Sensitivity, specificity, overall accuracy, positive and negative predictive values, positive and negative likelihood ratio, and diagnostic odds ratio and its 95% confidence intervals were calculated. The frequencies or ratios were compared using chi-square statistical criterion; the data with normal distribution were characterized by mean and with nonnormal distribution were characterized by median.

Results

During study period, 183 patients were enrolled into the study. There were 127 boys and 56 girls with a mean age of 10.3 years (SD, 3.8). AHO was diagnosed in 156 (85.2%) cases. Nineteen (10.4%) had arthritis, other purulent diseases were present in 5 (2.7%) cases, and 3 (1.6%) patients had other diseases. Most of the patients (68.3%) underwent 2 or 3 different radiologic investigations. One radiologic examination was performed in 4.9% of the patients, and 5 or more investigations were done in 10.9% of the cases. The characteristics of the entire group are shown in Table 1.

One hundred sixty-nine early x-rays (median test day, the first day of hospital stay) and 142 late x-rays (median test day, 15th day of hospital stay) were performed. The frequency (prevalence) of AHO in those groups was 0.86 and 0.92, respectively. Eighty-two ultrasonographies (median test day, the second day) were performed. The frequency of AHO in those patients was 0.79; pathologic changes were seen in 66.1% of the patients. Majority of the patients (91.2%) had pathologic changes in 76 bone scintigraphies with Tc99 (median, the third day; frequency of AHO, 0.76); 83.9% of the patients had pathologic changes in 38 MRIs (median, the seventh day; frequency of AHO, 0.83). Seventeen CTs were performed (median, the 10th day; frequency of AHO, 0.88). The pathologic changes were in 73.3% of the patients.

Sensitivity, specificity, overall accuracy, positive and negative predictive values, positive and negative likelihood ratio, and diagnostic odds ratio and its 95% confidence intervals are presented in Table 2.

Table 1. **The characteristics of study group**

Number of the patients	183
Male-to-female ratio	2.27:1
Age in years, mean (SD), range	10.3 (3.8), 1–17
Number of AHO cases (% of all)	156 (85)
Other diseases (% of all)	27 (15)
Number of early x-rays (1st day)	169
Number of ultrasonographies (2nd day)	82
Number of scintigraphies (3rd day)	76
Number of MRIs (7th day)	38
Number of CTs (10th day)	17
Number of late x-rays (15th day)	142
Number (%) of different investigations per patient	
1	9 (4.9)
2	80 (43.7)
3	45 (24.6)
4	29 (15.9)
5	16 (8.7)
6	4 (2.2)
Median disease duration until hospitalization, days	3
Hospital stay, mean (SD), days	29.9 (12.3)
Surgery frequency, %	64

AHO – acute hematogenous osteomyelitis; MRI – magnetic resonance imaging; CT – computed tomography; CD – standard deviation.

Table 2. **Diagnostic accuracy of different radiologic imaging methods in acute hematogenous osteomyelitis**

Method	Sensitivity (95% CI)	Specificity (95% CI)	Overall accuracy (95% CI)	PPV (95% CI)	NPV (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Diagnostic odds ratio (95% CI)
US	0.55 (0.43–0.67)	0.47 (0.24–0.7)	0.54 (0.43–0.64)	0.82 (0.71–0.93)	0.19 (0.06–0.32)	1.04 (0.62–1.74)	0.96 (0.53–1.75)	1.08 (0.30–3.84)
US for complications	0.74 (0.51–0.88)	0.95 (0.86–0.98)	0.9 (0.84–0.97)	0.82 (0.64–1.0)	0.92 (0.86–0.99)	15.23 (4.89–47.43)	0.28 (0.13–0.59)	55.07 (11.74–258.3)
CT	0.67 (0.38–0.88)	0.5 (0.01–0.98)	0.65 (0.42–0.87)	0.91 (0.74–1.0)	0.17 (0–0.46)	1.33 (0.32–5.58)	0.67 (0.14–3.17)	2.0 (0.02–172.4)
Early x-rays	0.16 (0.1–0.23)	0.96 (0.78–1.0)	0.27 (0.21–0.34)	0.96 (0.88–1.0)	0.16 (0.1–0.22)	3.81 (0.54–26.9)	0.88 (0.79–0.98)	4.34 (0.63–186.3)
MRI	0.81 (0.64–0.93)	0.67 (0.22–0.96)	0.79 (0.66–0.92)	0.93 (0.83–1.0)	0.4 (0.1–0.7)	2.44 (0.78–7.65)	0.28 (0.11–0.7)	8.67 (0.91–108.5)
Late x-rays	0.82 (0.75–0.88)	0.92 (0.62–1.0)	0.83 (0.77–0.89)	0.99 (0.97–1.0)	0.32 (0.17–0.48)	9.88 (1.56–20.1)	0.19 (0.13–0.29)	51.17 (6.61–2222.0)
Scintigraphy	0.81 (0.68–0.90)	0.84 (0.60–0.97)	0.82 (0.73–0.9)	0.94 (0.87–1.0)	0.59 (0.41–0.78)	5.11 (1.79–14.44)	0.23 (0.13–0.4)	22.3 (4.90–132.7)

CI – confidence interval; US – ultrasonography; CT – computed tomography; MRI – magnetic resonance imaging; PPV – positive predictive value; NPV – negative predictive value.

The sensitivity of early x-rays was significantly lower than sensitivity of all other radiologic tests ($P<0.05$). There were no significant differences in sensitivity and specificity of MRI, CT, and scintigraphy. The sensitivity of ultrasonography was significantly lower than sensitivity of MRI and scintigraphy ($P<0.05$), but its specificity was significantly lower only than the specificity of scintigraphy.

The diagnostic odds ratios of all imaging methods with the time of their performance are presented in Fig. 2

Discussion

It is very important to define diagnostic criteria of final diagnosis while we are studying diagnostic accuracy. There are different diagnostic criteria for AHO in the medical literature (8, 10). In this study, as well as in daily work, we have used our own criteria (3, 11, 12), which are quite similar to those described in references.

Analyzing diagnostic accuracy, we have used dichotomous evaluation – the disease is present or absent. But most of the radiologic diagnostic tests are valuable also in detecting localization, course, complications and results of treatment, in choosing proper treatment tactics. Therefore, our results are presented only for establishing the AHO diagnosis, and they do not reflect the value of the radiologic test generally.

We studied the accuracy of diagnostic methods in the group, where AHO is already suspected; therefore, prevalence of the disease was high in this group, and there are a relatively large number of tests showing true-positive results. If the prevalence of the disease in study group is low, there are more tests with true-negative results, and the predictive value is different. Positive and negative likelihood ratio is not dependent on prevalence of the disease and can show the accuracy better. A diagnostic odds ratio reflects the accuracy of the test for both confirming and denying diagnosis.

Peltola et al. in Finland studied the group of 50 patients with AHO. X-ray changes were found in 19% of cases already at the beginning of the treatment, 68% had changes on the 29th day of treatment, and 23% after one year (13). Kao et al. indicated that 67% of patients with septic arthritis and 53% of patients with AHO had no x-ray changes at the onset of the disease (14). The destructive changes in flat bones develop 2 or 3 weeks later than in long bones (15). Karwowska et al. found that 57% of x-rays performed at the beginning of the disease showed no changes (16). Just soft tissue swelling was seen in 15.9% and bone destruction in 12.4% of the cases.

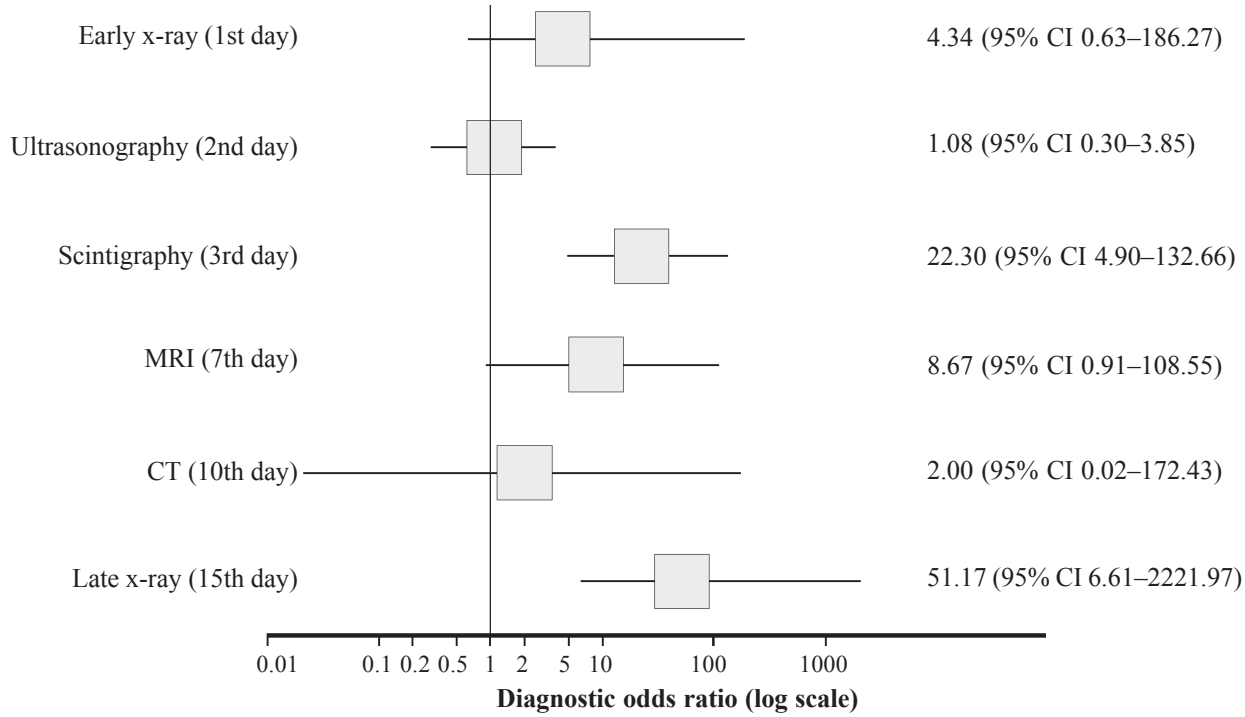

Fig. 2. **Diagnostic odds ratio and timing of different radiologic imaging methods in acute hematogenous osteomyelitis**

In our patients' group, early x-rays were performed on the first day of hospital stay, the median third day after the onset of the disease. The pathologic changes were seen in 26.8% of patients with AHO. The changes in the bone (destruction of the bone or thickening of the periosteum) and joint or soft tissues were detected in 16.2% and 10.6% of patients, respectively. The sensitivity of early x-rays, of course, was low (0.16), but specificity (0.96), positive predictive value (0.96), positive likelihood ratio (3.81), and high diagnostic odds ratio (4.34) were high. Those results contradict the opinion that in suspected osteomyelitis, plain x-rays are not reasonable. According to our data and studies from the literature, the pathologic changes on early x-rays are seen in 19% to 47% of all AHO patients; therefore, early x-rays have a significant diagnostic importance. When several tests are performed to the same patient, the probability of confirming or denying diagnosis increases (17). Early x-rays together with ultrasonography (parallel testing) increase overall sensitivity. Plain x-rays and ultrasonography are inexpensive methods, and it is possible to perform them on the first day of hospital stay; therefore, both are important methods especially when they are performed together.

There are a lot of studies about the advantages of bone scintigraphy in the diagnosis of AHO. Aronson et al. studied 50 children with unknown reason of limping (18). Scintigraphy detected the disease focus in 54% of patients; there were only 2 false-positive and 1 false-negative results. Tuson et al. analyzed the sensitivity and specificity of bone scan detecting musculoskeletal infections (19). The sensitivity of scintigraphy was 92%; specificity, 40%; positive predictive value, 86%; and negative predictive value, 63%. Karwowska et al. found that the sensitivity of scintigraphy with Tc99 was 93.9% (16). According to the data of Kaiser et al., the sensitivity and specificity of bone scintigraphy were 88% and 70%, respectively. The authors examined 65 patients (20). Weber-Chrysochoou et al. reported the sensitivity of 100% in case of pelvic osteomyelitis (21).

Our results are similar to the results of other studies. When comparing all the tests, the sensitivity, specificity, overall accuracy, positive and negative predictive values, positive and negative likelihood ratio, and diagnostic odds ratio of bone scintigraphy were the highest. Scintigraphy showed pathologic changes in 91% of patients with osteomyelitis. Those changes are present already at the beginning of the disease. We performed the test on the third day of hospital stay, the sixth day after the onset of the disease. Using

scintigraphy, the diagnosis could be established even on the first day of hospital stay. However, scintigraphy is less informative in anatomic and structural evaluation and mainly it is performed in purpose to find or to confirm the focus of infection in the bone.

CT can diagnose bone destruction very exactly, but it is not the most important test in the diagnosis of AHO. As on plain x-rays, the pathologic changes appear later, about 2 weeks after the beginning of the disease, and by this time, it is possible to notice bone destruction already on plain x-rays. However, CT might find soft tissue abscesses and AHO focuses in pelvis and vertebra or when underlying bones hide changes on plain x-rays (22).

In our study, CT was performed most rarely, totally only in 17 patients; therefore, sensitivity and specificity cannot be accurate. Several additional false-negative or false-positive results can change calculated accuracy dramatically. CT was performed when diagnosis remained unclear after other investigations. Undoubtedly, if CT would be done routinely, as late x-ray, overall accuracy would be high, higher than of plain x-ray. In clinical practice, this method is more important for the evaluation of treatment and its results when no pathologic changes are seen on plain x-ray.

MRI can help to show not only changes in the bones but soft-tissue pathology as well – accumulation of fluid, abscesses, also discitis, sacroiliitis – when other imaging methods cannot help. The main disadvantages of MRI are higher costs of the investigation and the need for sedation performing the test in smaller (younger than 4–5 years) children (21). The sensitivity and sensitivity of MRI, reported in other studies, range from 82% to 100% and from 75% to 96%, respectively (23).

According to data of our study, MRI is sensitive and specific (0.81 and 0.67), but does not reach the level, which is reported in other studies. Diagnostic odds ratio of MRI (8.67) is the third after scintigraphy and late x-rays, but this test is informative much earlier than late x-rays, so its early accuracy is just after scintigraphy. MRI is performed in unclear cases when other methods cannot confirm the diagnosis of AHO. The accuracy of MRI can be higher if done more frequently, not only in unclear and difficult cases. Other disadvantages of MRI are limited possibilities to perform the test urgently. The possibility to perform MRI on the first days of hospital stay together with other radiologic tests would make their parallel sensitivity close to 100% with a very high specificity too. MRI can help to define correct treatment tactics early, and the surgeon can avoid unnecessary operation as well as delayed surgery.

In the last decade, there were a lot of articles about usefulness of ultrasonography in the diagnosis of AHO (24–35). Prof. Siaurusaitis et al. in Vilnius studied the application of ultrasound in diagnosis of bone and joint diseases using conventional ultrasonography and performed measurements of the speed of ultrasound in bones (8, 36). They found very high, close to 100%, sensitivity and specificity of those methods.

It is rather difficult to evaluate the sensitivity and specificity of ultrasound in the diagnosis of AHO. Indirect symptoms of AHO are seen more often (fluid in the joint, soft tissue swelling); therefore, it is difficult to define whether test is true positive or negative, false positive and negative. We considered fluid in the joint as a true-positive result. Edema of the soft tissue was considered as false negative. Other considerations can change calculated accuracy dramatically.

If there are no changes in ultrasonography, the diagnosis of AHO cannot be excluded. Our results show a negative predictive value of 0.24, negative likelihood ratio very close to 1 (0.96), and diagnostic odds ratio of only 1.08. According to our data, ultrasonography alone is not very valuable in the diagnosis of AHO, but together with other methods, using parallel or consecutive testing, final accuracy increases. Different results were obtained when we calculated the accuracy of ultrasonography not for AHO, but for the complications of AHO, such as thickening of the periosteum, or pus accumulation under the periosteum, or pus accumulation in soft tissues. This diagnostic accuracy you can see in Table 2. It is characterized by high sensitivity, specificity, likelihood and odds ratios. The presence of subperiosteal abscess or soft tissue abscess defines the tactics of the treatment, and it is the indication for surgery. It is difficult to diagnose those complications clinically often, so high accuracy of ultrasound makes this method very valuable.

Conclusions

According our study, late x-rays is the most accurate radiologic imaging method in the diagnosis of acute hematogenous osteomyelitis in children, and bone scintigraphy and magnetic resonance imaging are the most accurate diagnostic methods at the onset of the disease.

Radiologinių tyrimų informatyvumas diagnozuojant vaikų ūminį hematogeninį osteomielitą

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Raktažodžiai: ūminis hematogeninis osteomielitas, diagnostinis tikslumas, jautrumas, specifiškumas, diagnostinis šansų santykis.

Santrauka. *Tyrimo tikslas*. Radiologinių tyrimų (rentgeno, echoskopijos, kaulų scintigrafijos, kompiuterinės tomografijos ir magnetinio rezonanso tomografijos) jautrumo, specifiškumo, tikslumo bei prognozinių teigiamojo, neigiamojo testų, tikimybinių verčių ir diagnostinių šansų santykio nustatymas ir palyginimas diagnozuojant vaikų ūminį hematogeninį osteomielitą.

Metodika. Atlikta perspektyvioji 2002–2008 m. Vaikų chirurgijos klinikoje gydytų vaikų, kuriems įtartas ūminis hematogeninis osteomielitas, ligos eigos duomenų analizė. Į tyrimą įtraukti 1–18 metų vaikai. Įtraukimo kriterijai: įtariamo židinio skausmas ir skausmingumas, sutrikusi funkcija, karščiavimas ir (ar) lokalios ar išplitusios bakterinės infekcijos požymiai. Šiems pacientams buvo atliktas rentgeno, echoskopijos, scintigrafijos, kompiuterinės tomografijos ir magnetinio rezonanso tomografijos tyrimas. Patvirtinus diagnozę, apskaičiuotas minėtų tyrimų jautrumas, specifiškumas ir diagnostinis šansų santykis, jų pasikliautinieji intervalai. Tyrimo metodikoje remtasi STARD (angl. *Standards for Reporting of Diagnostic Accuracy*) rekomendacijomis.

Rezultatai. Į tyrimą įtraukti 183 pacientai (127 berniukai, 56 mergaitės), amžiaus vidurkis – 10,3±3,8 metų; 156 (85 proc.) iš jų diagnozuotas ūminis hematogeninis osteomielitas, 27 (15 proc.) kitos ligos. Atlikta 169 ankstyvųjų (atlikimo laiko mediana – 1-oji gydymo diena) ir 142 vėlyvųjų (15-oji diena) rentgenologinių tyrimų, 82 echoskopijos (antroji diena), 76 kaulų scintigrafijos (trečioji gydymo diena), 38 magnetinio rezonanso tomografijos (7-oji diena) ir 17 kompiuterinės tomografijos tyrimų (10-oji diena). Apskaičiuotasis echoskopijos jautrumas – 0,55 (95 proc. PI 0,43–0,67), specifiškumas – 0,47 (0,24–0,7), diagnostinis šansų santykis – 1,08 (0,3–3,84). KT jautrumas – 0,67 (95 proc. PI 0,38–0,88), specifiškumas – 0,5 (0,01–0,98), diagnostinis šansų santykis – 2,0 (0,02–172,4). Ankstyvosios rentgenogramos jautrumas – 0,16 (95 proc. PI 0,1–0,23), specifiškumas – 0,96 (0,78–1,0), diagnostinis šansų santykis – 4,34 (0,63–186,3). MRT jautrumas – 0,81 (95 proc. PI 0,64–0,93), specifiškumas – 0,67 (0,22–0,96), diagnostinis šansų santykis – 8,67 (0,91–108,5). Vėlyvojo rentgenologinio tyrimo jautrumas – 0,82 (95 proc. PI 0,75–0,88), specifiškumas – 0,92 (0,62–1,0), diagnostinis šansų santykis – 51,17 (6,61–2222,0). Kaulų scintigrafijos jautrumas – 0,81 (95 proc. PI 0,68–0,90), specifiškumas – 0,84 (0,60–0,97), diagnostinis šansų santykis – 22,30 (4,9–132,7).

Išvados. Mūsų tyrimo duomenimis, diagnozuojant vaikų ūminį hematogeninį osteomielitą, informatyviausi yra vėlyvieji rentgeno tyrimai, o ligos pradžioje – kaulų scintigrafija ir magnetinio rezonanso tomografija.

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