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骨密度检测对婴幼儿佝偻病早期诊断的临床意义 *

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摘要 目的：探讨骨密度检测在佝偻病早期诊断中的应用价值。**方法：**收集衡水市哈励逊国际和平医院门诊诊治的600例婴幼儿，以血清维生素D3<27.5 nmol/L为判定标准分为非佝偻病组和佝偻病组，比较两组婴幼儿维生素D3、骨碱性磷酸酶和骨密度，绘制维生素D3、骨碱性磷酸酶、骨密度诊断结果的ROC曲线图，对骨密度检测结果进行评价。**结果：**佝偻病组婴幼儿维生素D3和骨密度Z值明显低于非佝偻病组，骨碱性磷酸酶显著高于非佝偻病组（P<0.05）。维生素D3诊断佝偻病的ROC曲线下面积为0.951，灵敏度为0.973，特异度为0.840；骨碱性磷酸酶诊断佝偻病的ROC曲线下面积为0.866，灵敏度为0.824，特异度为0.747；骨密度Z值诊断佝偻病的ROC曲线下面积为0.923，灵敏度为0.826，特异度为0.875，骨密度指标诊断佝偻病的曲线下面积和维生素D3比较无统计学意义（P>0.05），但骨密度指标诊断佝偻病的曲线下面积大于骨碱性磷酸酶（P<0.05）。**结论：**超声骨密度检测在婴幼儿佝偻病早期诊断中具有一定价值，其诊断敏感性、特异性、准确率与维生素D3诊断基本相当，且骨密度检测存在无创、可重复性高等优点。

关键词：佝偻病；维生素D3；骨碱性磷酸酶；骨密度

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Clinical Significance of Bone Mineral Density Measurement for the Early Diagnosis of Infant Rickets*

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ABSTRACT Objective: To explore the application value of bone mineral density test in early diagnosis of rickets. **Methods:** 600 infants and young children diagnosed and treated in the outpatient department of Harrison International Peace Hospital in Hengshui City were collected and divided into non-rickets group and rickets group with serum vitamin D3<27.5 nmol/L as the criterion. vitamin D3, bone alkaline phosphatase and bone mineral density of the infants and young children in the two groups were compared, ROC curves of diagnosis results of vitamin D3, bone alkaline phosphatase and bone mineral density were drawn, and the bone mineral density test results were evaluated. **Results:** Vitamin D 3 and bone mineral density Z values of infants in rickets group were significantly lower than those in non-rickets group, and bone alkaline phosphatase was significantly higher than that in non-rickets group (P<0.05). The area under ROC curve of vitamin D3 in the diagnosis of rickets was 0.951, the sensitivity was 0.973, and the specificity was 0.840. The area under ROC curve of bone alkaline phosphatase in the diagnosis of rickets was 0.866, the sensitivity was 0.824, and the specificity was 0.747. The area under ROC curve for diagnosing rickets with bone density Z value was 0.923, the sensitivity was 0.826, and the specificity was 0.875. There is no statistical significance between the area under curve for diagnosing rickets with bone density index and vitamin D3(P>0.05), but the area under the curve of bone mineral density index in diagnosis of rickets was larger than that of bone alkaline phosphatase (P<0.05). **Conclusion:** Ultrasonic bone density detection has certain value in the early diagnosis of infantile rickets. Its diagnostic sensitivity, specificity and accuracy are equal to vitamin D3 and bone density detection with the advantages of non-invasive and high repeatability.

Key words: Rickets; Vitamin D3; Bone alkaline phosphatase; Bone mineral density

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前言

佝偻病高是以体内维生素D缺乏为病理基础，钙磷代谢异常、骨矿化不全、神经肌肉免疫功能低下为临床特征的慢性

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营养不良疾病，多发于 2 周岁以下婴幼儿，严重影响婴幼儿生长发育[1,2]。流行病学调查研究显示[3,4]近年来佝偻病的发生率呈上升趋势。婴幼儿佝偻病的早期临床诊断方法较多，以 X 线片诊断，抽血钙元素含量、磷元素含量、骨碱性磷酸酶浓度、25- 羟维生素 D3 含量诊断等较为常见，但 X 线片对佝偻病的早期诊断价值不大，仅在骨矿含量丢失超过 30%时产生变化，实验室相关指标诊断属有创诊断，在婴幼儿应用中有一定难度[5,6]。因此，找寻一种快捷、无痛，且具有一定诊断准确率婴幼儿佝偻病早期诊断方法有重要作用。

骨密度检测仪主要用于检测人体骨矿含量，具有检测速度快、无创、无痛等特点，且测量数据 Z 值可较为准确的反映人体骨密度[7]。近年来，研究表明骨密度是婴幼儿早期佝偻病诊断的敏感指标[8]，但其诊断准确性与佝偻病诊断经典指标维生素D3、骨碱性磷酸酶的诊断准确性比较缺乏系统、全面的报道。本研究应用骨密度检测仪测定佝偻病患儿的骨密度，并探讨骨密度检测在佝偻病早期诊断中的应用价值，以期为佝偻病的早期诊断提供参考依据。

1 对象与方法

1.1 研究对象

选取 2017 年 9 月 ~2018 年 3 月在衡水市哈励逊国际和平医院门诊就诊的 600 例婴幼儿作为研究对象，入选标准：行血清维生素 D3 水平检测；年龄 3 个月 ~2 岁；征得受试者家长知情同意。排除标准：有明显骨骼系统发育异常、肝肾疾病及癫痫婴幼儿，近期接受维生素 D、生长激素等药物。参照婴幼儿早期佝偻病诊断标准[9]，将就诊的 600 例婴幼儿分为佝偻病组和非佝偻病组，两组婴幼儿的临床基线资料比较无统计学意义（P>0.05），有可比性，见表 1。

表 1 非佝偻病组和佝偻病组临床基线资料比较

Table 1 Comparison of clinical baseline data between non-rickets group and rickets group

Groups	n	Percentage of boys (%)	Average age (one year old)	Average height (cm)	Average weight (kg)
Non-rickets group	526	274(52.09)	1.14± 0.34	63.64± 6.84	14.65± 3.21
Rickets group	74	40(54.05)	1.18± 0.31	64.12± 6.79	14.34± 3.18
tor x^2		0.037	0.957	0.566	0.779
P		0.178	0.074	0.091	0.083

1.2 研究方法

比较两组婴幼儿骨密度检测 Z 值、血清骨碱性磷酸酶含量、血清维生素 D3 浓度差异，并以 " 维生素 D3<27.5 nmol/L" 为婴幼儿佝偻病早期诊断金标准，绘制骨密度、骨碱性磷酸酶诊断结果的 ROC 曲线图。

1.2.1 指标检测方法 采用 MAGLUMI 2000 检测维生素 D3 水平，试剂盒购自深圳新产业生物医学公司。采用美国 Elx800 全自动酶标仪检测骨碱性磷酸酶浓度，试剂盒由美国 METRA 公司提供。采用 SunlightOmnisense 7000P 型骨密度仪检测所有受试者胫骨中上三分之一段的骨密度。

1.2.2 ROC 曲线图绘制及评价 绘制维生素 D3、碱性磷酸酶浓度和骨密度值对佝偻病诊断的 ROC 曲线图，以曲线最接近左上角的点作为最优临界点，取最优临界点的纵坐标为检测灵敏度、横坐标为检测特异性，线下面积表示准确度[9]，对维生素 D3、碱性磷酸酶浓度和骨密度值诊断结果进行评价。

1.3 统计学方法

数据处理选用 SPSS18.0 软件包，计量资料用（$\bar{x}\pm s$）表示，组间比较选用 t 检验，计数资料用[例(%)]表示，组间比较用 x^2 检验比较，采用受试者工作特征曲线(ROC)分析骨碱性磷酸酶和骨密度对佝偻病的诊断价值，曲线下面积比较采用 Z 检验，以 P<0.05 表示差异有统计学意义。

2 结果

2.1 两组婴幼儿维生素 D3、骨碱性磷酸酶和骨密度的比较

佝偻病组婴幼儿维生素 D3 和骨密度 Z 值低于非佝偻病组，骨碱性磷酸酶高于非佝偻病组（P<0.05），见表 2。

表 2 两组婴幼儿维生素 D3、骨碱性磷酸酶和骨密度的比较（$\bar{x}\pm s$）

Table 2 Comparison of the Vitamin D3, bone alkaline phosphatase and bone mineral density between two groups of infants（$\bar{x}\pm s$）

Groups	n	Vitamin D3 (nmol/L)	Bone alkaline phosphatase (u/L)	Bone mineral density z value
Non-rickets group	526	45.79± 6.31	186.67± 10.44	2.54± 0.43
Rickets group	74	25.63± 4.19	27837.54± 198.72	0.88± 0.11
t		26.659	3176.299	33.035
P		0.000	0.000	0.000

2.2 婴幼儿骨碱性磷酸酶和骨密度对佝偻病的诊断价值分析

用 ROC 曲线评价维生素 D3、骨碱性磷酸酶和骨密度对佝偻病的诊断价值，结果显示：维生素 D3 诊断的 ROC 曲线下面积为 0.951，灵敏度为 0.973，特异度为 0.840；骨碱性磷酸酶 ROC 曲线下面积为 0.866，灵敏度为 0.824，特异度为 0.747；骨密度 Z 值的 ROC 曲线下面积为 0.923，灵敏度为 0.826，特异度

为 0.875，骨密度指标诊断的曲线下面积和维生素 D3 比较无统计学意义(P>0.05)，但骨密度指标诊断的曲线下面积大于骨碱性磷酸酶(P<0.05)，见表 3、4。

表 3 维生素 D3、骨碱性磷酸酶和骨密度对佝偻病的诊断价值分析

Table 3 Diagnostic value of vitamin D 3, bone alkaline phosphatase and bone mineral density for rickets

Indicators	Area	SE	Sig	95%CI		Sensitivity	Specificity
				Lower limit	Upper limit		
Vitamin D3	0.951	0.009	0.000	0.934	0.969	0.973	0.840
Bone alkaline phosphatase	0.866	0.024	0.000	0.818	0.913	0.824	0.747
Bone mineral density z value	0.923	0.015	0.000	0.894	0.952	0.826	0.875

表 4 维生素 D3、骨碱性磷酸酶和骨密度对佝偻病诊断的 ROC 曲线下面积比较

Table 4 Comparison of area under roc curve of vitamin D _ 3, bone alkaline phosphatase and bone mineral density in diagnosis of rickets

Indicators	z	P
Vitamin D3 vs Bone mineral density z value	1.601	0.055
Bone mineral density z value vs. Bone alkaline phosphatase	2.014	0.022

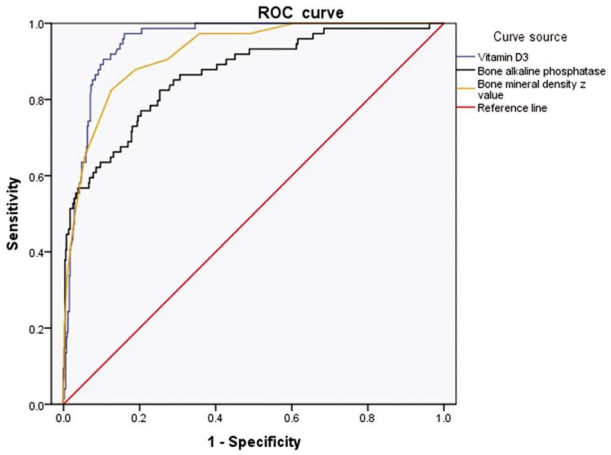

图 1 维生素 D3、骨碱性磷酸酶和骨密度对佝偻病诊断的 ROC 曲线分析

Fig.1 ROC curve analysis of vitamin D3, bone alkaline phosphatase and bone mineral density in diagnosis of rickets

3 讨论

佝偻病多见于 3 月～2 周岁婴幼儿，此时婴幼儿生长发育迅速，体内钙、磷元素含量及营养状况可导致婴幼儿骨发育异常，从而导致佝偻病发生，同时由于婴幼儿生长发育中佝偻病导致骨骼改变，容易影响婴幼儿神经兴奋性及病变骨骼部位肌肉发育。因此，随着病情发展，佝偻病在不同年龄阶段会有一定的差异性[10,11]。食物中维生素 D 摄入量不足，生长发育太快，日照时间不足，围生期母体维生素 D 摄入不足等均是婴幼儿佝偻病发生的内源因素[12,13]，慢性腹泻、肝炎综合征、肝肾功能不全等外源性因素也可导致婴幼儿佝偻病发生[14]。佝偻病的临床分期主要包括初期(早期)、活动期(发展期)和后遗症期，早期临床以神经兴奋表现为主，多出现多汗、哭闹、摇头、易激、易怒等症状，此时与健康婴幼儿相比，血清维生素 D3 会显著下降，骨碱性磷酸酶会显著提升[15,16]。活动期是病情发展加重期，此时婴幼儿会出现机体磷、钙代谢失常，成骨细胞功能亢进等变化，且小于 6 月龄婴幼儿以颅骨病变为主，其次为肋骨与肋软骨病变，尽管婴幼儿经充足阳光照射及临床治疗后症状可改善或消失，但仍有部分幼儿发展到后遗症期，最终导致婴幼儿出现不同程度的骨骼畸形[17]。因此，早期诊断在婴幼儿佝偻病临床防治中具有重大意义。

婴幼儿佝偻病的早期临床诊断方法较多，X 线检查易对患儿形成潜在放射性损害，且特异性不高。25(OH)D3 作为人体维生素 D 的代谢产物，其半衰期较长，血钙、血磷、甲状旁腺素对其影响较小，同时也可反映机体维生素 D 摄入量和阳光照射维生素 D 产生量，因此有研究认为 25(OH)D3 含量测定可作为婴幼儿佝偻病早期诊断的敏感指标[18,19]。骨碱性磷酸酶是成骨细胞合成的重要影响因素，婴幼儿机体维生素 D 浓度下降，骨碱性磷酸酶活浓度上升时，成骨细胞活跃性较高，从而诱发婴幼儿佝偻病[20,21]。有关研究显示[22,23]婴幼儿佝偻病早期血清检验中，骨碱性磷酸酶异常率高达 96.77%，可作为婴幼儿佝偻病早期诊断的敏感指标。有关研究将维生素 D 和钙同时作为佝偻病的发病原因，指出佝偻病发生不仅和维生素 D 缺乏有关，且钙元素与婴幼儿骨骼成长密切相关[24,25]。因此，骨密度检测指标可能为婴幼儿佝偻病早期诊断的敏感指标[26]。本研究结果显示：与非佝偻病组比较，佝偻病组婴幼儿骨密度检测 Z 值和维生素 D3 浓度偏低，骨碱性磷酸酶浓度偏高，提示骨密度检测指标可能为婴幼儿佝偻病早期诊断提高参考依据。

血清骨碱性磷酸酶及 25 (OH)D3 在婴幼儿佝偻病早期诊断中的价值已得到相关研究证实[27]。本研究结果显示骨密度指标诊断的 ROC 曲线下面积与维生素 D3 相似，但骨密度指标诊断的 ROC 曲线下面积大于骨碱性磷酸酶，提示超声骨密度检测在婴幼儿佝偻病早期诊断中具有具有一定的价值，其诊断价值与维生素 D3 诊断基本相当，与 Mikiko Ito 等[28]的研究结论吻合。Thomas H 等[29]研究也表明骨密度检测仪在预防早期佝偻病筛查中具有重要的价值，其可更早地诊断出佝偻病，从而给予婴儿早期佝偻病更早的临床治疗。Harada D 等[30]认为骨密度测定不仅可用于婴幼儿骨骼生长发育检查，且在婴幼儿早期佝偻病诊断中具有高度特异性。

综上所述,超声骨密度检测在婴幼儿佝偻病早期诊断中具有一定价值,其诊断敏感性、特异性、准确率与维生素 D3 诊断基本相当,但骨密度检测存在无创、可重复性高等优点。

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