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钼靶 X 线摄片联合肿瘤相关标志物检测对乳腺癌的诊断价值

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摘要 目的:探讨乳腺钼靶 X 射线摄片与血清糖类抗原 15-3(CA15-3)、癌胚抗原(CEA)和骨桥蛋白(OPN)联合检测对乳腺癌的临床诊断价值。**方法:**选择在我院经手术和病理证实为乳腺癌的患者 60 例作为研究组,另选取 60 例健康体检者作为对照组。分别检测两组的血清 CA15-3、CEA 和 OPN 水平,并采用乳腺钼靶 X 射线检查。比较 X 射与血清学检测单独检测及联合检测的阳性率。**结果:**研究组患者血清 CA15-3、CEA 及 OPN 水平均显著高于对照组,差异具有统计学意义($P<0.05$);血清 CA15-3、CEA、OPN 和钼靶 X 射线摄片联合检测的敏感性显著高于单独检测,差异具有统计学意义($P<0.05$)。**结论:**对乳腺癌患者进行钼靶 X 射线摄片及肿瘤相关标志物检测可提高阳性检出率,有利于乳腺癌的早期诊断及治疗。

关键词:乳腺癌;钼靶 X 射线;肿瘤相关标志物;血清学检查

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Diagnostic Value of X-ray Combined with Detection of Tumor-related Markers in Serum of Breast Cancer

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ABSTRACT Objective: To investigate the diagnostic value of mammography X-ray radiography and serum detection of carbohydrate antigen 15-3 (CA15-3), carcinoembryonic antigen (CEA) and osteopontin (OPN) for breast cancer. **Methods:** 60 cases with breast cancer who were treated in our hospital were selected as the study group, and 60 healthy volunteers were selected as a control group. The two groups were detected in serum CA15-3, CEA and OPN levels and the use of mammography X-ray examination. Comparison of X-ray-positive rate and serology testing and joint detection alone. **Results:** The study group serum CA15-3, were significantly higher than CEA and OPN water, the difference was statistically significant($P<0.05$); serum CA15-3, CEA, OPN and mammography X-ray radiography combined detection significantly higher detection sensitivity alone, the difference was statistically significant ($P<0.05$). **Conclusion:** Radiography and tumor-associated markers for breast cancer patients concluded the X-ray mammography can increase the positive detection rate for early diagnosis and treatment of breast cancer.

Key words: Breast cancer; X-ray; Tumor-related Markers; Serum detection

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前言

乳腺癌(Breast cancer)是严重危害女性健康的恶性肿瘤,发病率和死亡率呈逐年上升趋势,多数患者确诊时肿瘤已发展为中晚期,预后较差。因此,对乳腺癌进行早期诊断和治疗是提高患者生存质量的关键^[1-3]。近年来,随着高清晰度数字化乳腺专用 x 射线的广泛应用,乳腺癌的诊断率显著提高,但该方法易受患者年龄的影响,且放射对身体有一定危害^[4,5]。此外,乳腺肿瘤相关标志物 CA15-3、CEA 和 OPN 的血清学辅助诊断虽然具有较高的准确性,但单项标记物检测易发生漏诊,诊断效果并不理想^[6,7]。因此,探索多项指标联合检测以提高准确率是目前临床研究的重点^[8]。本研究对 2012 年 10 月至 2014 年 2 月在

我院确诊为乳腺癌患者的 x 线片和肿瘤标志物检测结果进行回顾性分析,以探讨乳腺钼靶 X 射线摄片及 CA15-3、CEA、OPN 血清学检测对乳腺癌的诊断价值,为肿瘤的早期治疗提供依据。

1 资料与方法

1.1 资料

选取 2012 年 10 月至 2014 年 2 月在我院经组织影像学诊断和术后病理证实确诊为乳腺癌的患者 60 例作为研究对象,患者均为女性,年龄 38-73 岁,平均 56.5 ± 11.2 岁。另选取同期进行体检未发现乳腺疾病及其他肿瘤的 60 位志愿者作为对照组,年龄 36-69 岁,平均 53.4 ± 12.6 岁,均无乳腺疾病史。两组基本资料无显著差异($P>0.05$),具有可比性。

1.2 方法

1.2.1 乳腺钼靶 X 射线 采用专用数字式乳腺 X 射线机摄片,术前先进行常规头尾位及侧斜位检查及拍摄,如无可疑特

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征则确立诊断,如两侧不对称疑有病灶者行局部放大摄影。乳腺癌的判定标准是:钼靶摄影片的征象包括乳腺癌的直接征象或间接征象。直接征象有肿块或结节、钙化;间接征象主要包括皮肤增厚和/或局限凹陷、乳头内陷和漏斗征、大导管征、伪足征及彗星尾征、牛角征等。

1.2.2 血清学检测 晨起空腹抽静脉血 3 mL,用促凝管采集,3000 r/min 离心 5 min,分离血清,用于检测 CA15-3、CEA 和 OPN,样本采集后 2 h 内上机检测。用化学发光免疫分析法检测 CA15-3 和 CEA,酶联法检测 OPN,操作步骤严格按照说明书进行。CA15-3 $\geq$ 28 U/ml,CEA $\geq$ 10 ng/ml 为阳性。

1.3 统计学处理

所有数据采用 SPSS16.0 统计软件进行分析处理。组间比较采用 t 检验或 fishert 检验,计数资料采用($\bar{x} \pm s$)表示,阳性率比较采用 检验, $\alpha=0.05$ 为检验水准,以 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 两组血清 CA15-3、CEA 和 OPN 水平比较

研究组患者血清 CA15-3、CEA、OPN 水平显著高于对照组,差异有统计学意义($P<0.05$),见表 1。

表 1 两组血清 CA15-3、CEA、OPN 比较($\bar{x} \pm s$)

Table 1 Comparison of CA15-3, CEA and OPN levels in serum of patients between two groups

Group	Case	CA15-3(U/mL)	CEA(ng/mL)	OPN(μ g/L)
Control group	60	7.9 $\pm$ 5.5	2.4 $\pm$ 1.1	10.2 $\pm$ 5.3
Study group	60	82.4 $\pm$ 8.2	28.4 $\pm$ 8.3	30.6 $\pm$ 7.9
t		16.081	20.125	13.897
P		0.00	0.00	0.00

2.2 两组乳腺钼靶 X 射线和各指标单项检测的阳性率比较

研究组乳腺钼靶 X 射线摄片及血清 CA15-3、CEA 和 OPN

检测的阳性率显著高于对照组,两组比较差异均有统计学意义($P<0.05$)。见表 2。

表 2 钼靶 X 射线片、CA15-3、CEA 和 OPN 单项检测阳性率[n(%)]

Table 2 Comparison of positive rate of detection by either the X ray or the related indexes in serum

Group	Case	CA15-3(U/mL)	CEA(ng/mL)	OPN(μ g/L)	X ray
Control group	60	2(3.33%)	3(5%)	0(0.0)	1(1.67%)
Study group	60	17(28.33%)	10(16.67%)	8(13.33%)	29(48.33%)
χ^2		21.263	12.343	-	-
P		0.000	0.000	0.280	0.000

2.3 单独检测和联合检测的阳性率比较

对照组 CA15-3+CEA+OPN 检测的阳性率为 3.33%(2/60),CA15-3+CEA+OPN 和钼靶 X 射线联合检测的阳性率为 3.33%(2/60);研究组 CA15-3+CEA+OPN 检测的阳性率为 55%(33/60),CA15-3+CEA+OPN 和钼靶 X 射线联合检测的阳性率为 63.33%(38/60)。研究组单项检测和联合检查的检出率均显著高于对照组,差异具有统计学意义($P<0.05$)。

3 讨论

乳腺钼靶 x 线摄影术是目前公认的检测早期乳腺癌的有效手段,特别是对微细钙化的显示,而微细钙化是 X 线诊断乳腺癌的重要征象^[9]。当 X 射线片上表现为典型的恶性钙化,虽无其它恶性征象相伴,亦可诊断为乳腺癌^[10]。肿块是乳腺癌最直接、最常见的 X 线征象,分叶、边缘毛刺、小尖角征等是诊断乳癌的重要征象^[11]。据研究证实,乳腺钼靶 x 线摄影术单项测定的阳性率为 66.7%,且乳腺高频钼靶 x 线检查具有简捷、有效、无创等优点^[12]。

CA15-3 属糖蛋白,是一种乳腺癌的相关抗原,存在于乳腺癌细胞中,乳腺癌细胞会将其释放到血液循环中。研究表明,CA15-3 对乳腺癌的早期诊断具有重要的临床意义^[13]。乳腺癌患

者血清 CA15-3 水平已被临床肯定为一种较为敏感的肿瘤标志物。CEA 是一种糖蛋白,也是较为广谱的血清肿瘤标志物之一,主要用于监测肿瘤发展,判断疗效和估计预后^[14]。相关研究表明,CEA 在胃癌、胰腺癌、乳腺癌、结肠癌和胆管癌中的含量可见增高^[15,16]。OPN 是一种磷酸化糖蛋白,也称转化相关性磷酸蛋白,在肿瘤的发生、转移中起重要的作用,它有明显促进肿瘤恶化的倾向^[17]。有研究表明,OPN 在肿瘤转移患者血清中的水平明显升高^[18,20]。因此,OPN 在细胞免疫应答、肿瘤发生及转移的作用备受关注^[19]。

结合本研究,研究组患者血清 CA15-3、CEA、OPN 水平显著高于对照组,研究组乳腺钼靶 X 射线摄片单独检查、血清 CA15-3、CEA 和 OPN 单独检测及两种方法联合检测的阳性率均显著高于对照组,且联合检测的检出率高于单独检测,差异具有统计学意义($P<0.05$)。结果说明,CA15-3、CEA、OPN 均可作为乳腺癌的辅助诊断指标,且联合检测可弥补单指标检测的不足,使乳腺癌的早期诊断率获得提高,对乳腺癌诊断具有重要意义。

因此,临床应采取多种方法联合检测乳腺癌以提高诊断的准确率,减少漏诊的发生。

参 考 文 献(References)

- [1] Gidcumb E, Gao B, Shan J, et al. Carbon nanotube electron field emitters for x-ray imaging of human breast cancer [J]. *Nanotechnology*, 2014, 25(24): 245704
- [2] Tengström M, Mannermaa A, Kosma VM, et al. XRCC1 rs25487 Polymorphism Predicts the Survival of Patients After Postoperative Radiotherapy and Adjuvant Chemotherapy for Breast Cancer[J]. *Anticancer Res*, 2014, 34(6): 3031-3037
- [3] Simonavice E, Liu PY, Ilich JZ, et al. The effects of a 6-month resistance training and dried plum consumption intervention on strength, body composition, blood markers of bone turnover, and inflammation in breast cancer survivors [J]. *Appl Physiol Nutr Metab*, 2014, 39(6): 730-739
- [4] Patel AS, Allen JE, Dicker DT, et al. Detection of circulating tumor cells in the cerebrospinal fluid of a patient with solitary metastasis from breast cancer: A case report [J]. *Oncol Lett*, 2014, 7 (6): 2110-2112
- [5] Wang Z, Hauser N, Singer G, et al. Non-invasive classification of micro calcifications with phase-contrast X-ray mammography [J]. *Nat Commun*, 2014, 5: 3797
- [6] Appleton DC, Hackney L, Narayanan S. Ultrasonography alone for diagnosis of breast cancer in women under 40[J]. *Ann R Coll Surg Engl*, 2014, 96(3): 202-206
- [7] Scimeca M, Giannini E, Antonacci C, et al. Micro calcifications in breast cancer: an active phenomenon mediated by epithelial cells with mesenchymal characteristics[J]. *BMC Cancer*, 2014, 14(1): 286
- [8] Li DL, Wei L, Wen XM, et al. The effects of X-ray irradiation on the proliferation and apoptosis of MCF-7 breast cancer cells [J]. *Ultrastruct Pathol*, 2014, 38(3): 211-216
- [9] Feng SS, D'Orsi CJ, Newell MS, et al. X-ray scatter correction in breast tomosynthesis with a precomputed scatter map library [J]. *Med Phys*, 2014, 41(3): 031912
- [10] Auweter SD, Herzen J, Willner M, et al. X-ray phase-contrast imaging of the breast--advances towards clinical implementation [J]. *Br J Radiol*, 2014, 87(1034): 20130606
- [11] Schleede S, Bech M, Grandl S, et al. X-ray phase-contrast tomosynthesis for improved breast tissue discrimination [J]. *Eur J Radiol*, 2014, 83(3): 531-536
- [12] Varshosaz J, Sadeghi-aliabadi H, Ghasemi S, et al. Use of magnetic folate-dextran-retinoic acid micelles for dual targeting of doxorubicin in breast cancer[J]. *Biomed Res Int*, 2013, 2013: 680712
- [13] Séradour B, Heid P, Estève J. Comparison of direct digital mammography, computed radiography, and film-screen in the French national breast cancer screening program[J]. *AJR Am J Roentgenol*, 2014, 202 (1): 229-236
- [14] Cole LE, Vargo-Gogola T, Roeder RK. Bisphosphonate-functionalized gold nanoparticles for contrast-enhanced X-ray detection of breast micro calcifications[J]. *Biomaterials*, 2014, 35(7): 2312-2321
- [15] Zhang H, Guo M, Chen JH, et al. Osteopontin knock down inhibits 3 integrin-induced cell migration and invasion and promotes apoptosis of breast cancer cells by inducing autophagy and inactivating the PI3K/Akt/mTOR pathway [J]. *Cell Physiol Biochem*, 2014, 33 (4): 991-1002
- [16] Bramwell VH, Tuck AB, Chapman JA, et al. Assessment of osteopontin in early breast cancer: correlative study in a randomised clinical trial[J]. *Breast Cancer Res*, 2014, 16(1): R8
- [17] Thorat D, Sahu A, Behera R, et al. Association of osteopontin and cyclooxygenase-2 expression with breast cancer subtypes and their use as potential biomarkers[J]. *Oncol Lett*, 2013, 6(6): 1559-1564
- [18] Shi Z, Mirza M, Wang B, et al. Osteopontin-a alters glucose homeostasis in anchorage-independent breast cancer cells [J]. *Cancer Lett*, 2014, 344(1): 47-53
- [19] Riccardi F, Mocerino C, Barbato C, et al. 18FDG-PET for early prediction of complete response to lapatinib and capecitabine in HER2-positive metastatic breast cancer: a case report [J]. *Tumori*, 2013, 99(6): 257e-60e
- [20] Koolen BB, WV Vogel, MJ Vrancken, et al. Molecular Imaging in Breast Cancer: From Whole-Body PET/CT to Dedicated Breast PET [J]. *J Oncol*, 2012, 2012: 438647