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双能量增强 CT 扫描对非小细胞肺癌纵隔淋巴结转移的诊断价值分析*

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摘要 目的:探讨双能量增强 CT 扫描诊断非小细胞肺癌(NSCLC)纵隔淋巴结转移的应用价值。**方法:**回顾性分析我院 2017 年 5 月至 2019 年 5 月接诊的 100 例行肺部双能量增强 CT 扫描的 NSCLC 患者临床资料,根据术后病理诊断是否发生纵隔淋巴结转移将患者转移组(42 例)和未转移组(58 例)。比较组间能谱曲线斜率(λ HU)、淋巴结与原发癌灶能谱曲线斜率比值(简称斜率比值)、碘浓度(IC)、水浓度(WC)、标准化碘浓度(NIC)、标准化水浓度(NWC)差异,Logistic 回归分析双能 CT 参数与 NSCLC 发生纵隔淋巴结转移的相关性,受试者工作特征曲线(ROC)分析双能 CT 参数诊断 NSCLC 发生纵隔淋巴结转移的效能。**结果:**转移组 λ HU、斜率比值、IC、NIC 均低于未转移组($P<0.05$),转移组 λ HU、IC、WC、NIC、NWC 与原发病灶比较均无统计学差异($P>0.05$),未转移组 λ HU、IC、NIC 高于原发病灶($P<0.05$)。Logistic 回归分析结果显示 λ HU、斜率比值、IC、NIC 均与纵隔淋巴结转移有关($P<0.05$)。ROC 分析结果显示 λ HU、斜率比值、IC、NIC 诊断 NSCLC 纵隔淋巴结转移的 AUC 分别为 0.849、0.871、0.838、0.860,灵敏度分别为 80.95%、85.71%、78.57%、83.33%,特异度分别为 79.31%、84.48%、81.03%、82.76%。**结论:**双能量增强 CT 扫描检查有助于提高 NSCLC 淋巴结转移准确率。

关键词:双能量增强 CT;非小细胞肺癌;纵隔淋巴结转移;能谱曲线;能谱曲线斜率;标准化碘浓度

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Dual-energy Enhanced CT Scan in the Diagnosis of Mediastinal Lymph Node Metastasis of Non-small Cell Lung Cancer*

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ABSTRACT Objective: To investigate the value of dual-energy enhanced CT in the diagnosis of mediastinal lymph node metastasis in non-small cell lung cancer (NSCLC). **Methods:** The clinical data of 100 NSCLC patients who were receiving dual-energy enhanced lung CT scan in our hospital from May 2017 to May 2019 were retrospectively analyzed. Patients were divided into the metastatic group (42 cases) and the non-metastatic group (58 cases) whether mediastinal lymph node metastasis occurs according to postoperative pathological diagnosis. The differences of the slope of the energy spectrum curve (λ HU), the ratio of the slope of the energy spectrum curve between lymph nodes and primary cancer foci (slope ratio for short), iodine concentration (IC), water concentration (WC), normalization iodine concentration (NIC), normalization water concentration (NWC) were compared. Logistic regression analysis was performed to analyze the correlation between dual-energy CT parameters and mediastinal lymph node metastasis in NSCLC, and the Receiver operator characteristics curve (ROC) was used to analyze the efficacy of dual-energy CT parameters in diagnosing mediastinal lymph node metastasis in NSCLC. **Results:** The λ HU, slope ratio, IC and NIC in the metastatic group were lower than those in the non-metastatic group ($P<0.05$). There was no significant difference of λ HU, IC, WC, NIC and NWC between the metastatic group and the primary lesion ($P>0.05$). The λ HU, IC and NIC in the non-metastatic group were higher than those in the primary lesion ($P<0.05$). Logistic regression analysis showed that λ HU, slope ratio, IC and NIC were all associated with mediastinal lymph node metastasis ($P<0.05$). ROC analysis results showed that the AUC of λ HU, slope ratio, IC and NIC in diagnosing mediastinal lymph node metastasis of NSCLC were 0.849, 0.871, 0.838, 0.860, respectively. The sensitivity were 80.95%, 85.71%, 78.57% and 83.33%, respectively, and the specificity was 79.31%, 84.48%, 81.03% and 82.76%, respectively. **Conclusion:** Dual-energy enhanced CT scan is helpful to improve the accuracy of NSCLC lymph node metastasis.

Key words: Dual-energy enhanced CT; Non-small cell lung cancer; Mediastinal lymph node metastasis; Energy spectrum curve; Energy spectrum curve; Normalization iodine concentration

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前言

非小细胞肺癌(Non-small-cell lung cancer, NSCLC)是临床最常见的肺癌类型,死亡率位居恶性肿瘤首位^[1,2]。尽管肺癌治疗取得了很大的进展,但是 NSCLC 患者 5 年生存率仍不到 18%^[3]。淋巴结转移是 NSCLC 诊断的难点和关键,对于临床诊疗方案拟定、疗效评估均有重要价值。CT 是无创评估淋巴结转移的主要影像诊断手段,既往临床以 CT 横轴位淋巴结短径 ≥ 10 mm 为诊断标准,但准确率偏低。经皮或经支气管镜穿刺淋巴结活检准确率高,但是该方法有创,无法对所有淋巴结进行诊断^[4,5]。双能量增强 CT 扫描获得能量图像可测量病变组织在不同能量下 CT 值变化,根据 CT 能谱曲线率定量判断病灶性质^[6,7],在淋巴结转移诊断方面颇具应用前景。目前双能量增强 CT 在 NSCLC 纵膈淋巴结转移诊断的研究不多,且无一致性结论和统一标准。鉴于此本研究回顾性收集了 100 例 NSCLC 患者双能量增强 CT 扫描资料,探讨双能量增强 CT 对 NSCLC 纵膈淋巴结转移的诊断价值。

1 资料与方法

1.1 临床资料

回顾性分析我院 2017 年 5 月至 2019 年 5 月接诊的 100 例例行肺部双能量增强 CT 扫描的 NSCLC 患者临床资料,患者纳入标准:① 经支气管镜或空芯针肺穿刺活检病理学证实为 NSCLC;② 均行双能量增强 CT 扫描,图像清晰,数据完整;③ 均行肺癌切除手术和纵膈淋巴结清扫手术,术后病理结果完整;④ 患者及其家属均知情同意签署同意书。排除标准:① 经病理证实为其它类型的肺癌;② 进行双能量增强 CT 扫描前已经接受放疗或化疗等形式治疗;③ 淋巴结直径过小无法测量、淋巴结钙化、坏死者。100 例 NSCLC 患者中男 69 例,女 31 例,年龄 52~67 岁,平均(62.35 $\pm$ 4.25)岁,TNM 分期:III 期 53 例,IV 期 47 例;病理类型:腺癌 59 例,鳞癌 41 例。本研究获得我院伦理会批准,诊疗过程严格遵循伦理学原则,保障患者隐私和安全。

1.2 双能量增强 CT 扫描方法^[8]

检查前签署知情同意书,排除碘过敏,指导患者进行呼吸屏气训练。Discovery HD 750 宝石能谱 CT 扫描仪(美国 GE 公司)行常规平扫(管电压 120 kVp,管电流 120 mAs,层厚 6 mm,层间距 5 mm,螺距 1.0,管球旋转时间 0.28 s)和双能量静脉期增强扫描[Liver VNC 序列,高低能量管电压分别为 140 kVp、80 kVp(瞬时切换),管电流 170 mAs、200 mAs,层厚 0.8 mm、

层间距 1.25 mm,准直器 64 $\times$ 0.6 mm,螺距 0.55,旋转时间 0.6s]。扫描前经肘静脉注射采用双筒高压注射器(美国 MEDRAD STELLANT CT)以 5~5.5 mL/s 速度团注对比剂碘普罗胺注射液(优维显,370 mg I/mL)80~100 mL,后注射生理盐水 40 mL。嘱患者深吸呼气末屏气,注射对比剂后 35s 开始增强扫描,扫描范围自肺尖至肺底。

1.3 图像处理^[3,9]

扫描图像经薄层重建导入 AW4.6 工作站,GSI View 双能量处理软件自动生成 40~140keV 图像,选择 70 keV 图像,以纵膈淋巴结密度相对均匀实性部分作为感兴趣区,避开血管、钙化及坏死部分。测量 40~140keV(每间隔 10keV)能量下病灶 CT 值、碘浓度(Iodine concentration, IC)、水浓度(Water concentration, WC)。CT 值变化曲线即能谱曲线,根据公式计算原发病灶、淋巴结能谱曲线斜率(λ HU),公式为 $\lambda = (CT_{40keV} - CT_{100keV})/60$,并计算纵膈淋巴结/原发病灶能谱曲线斜率比值(以下简称斜率比值)。计算标准化碘浓度(Normalization iodine concentration, NIC)、标准水浓度(Normalization water concentration, NWC),NIC=原发病灶 IC/同层面降主动脉或锁骨下动脉 IC, NWC=原发病灶 WC/同层面降主动脉或锁骨下动脉 WC。由我院 10 年以上 CT 工作经验医师进行操作和测量。

1.4 统计学分析

SPSS 25.0 进行数据分析, λ HU、斜率比值、IC、WC、NIC、NWC 比值均经 Kolmogorov-Smirnov 检验,符合正态分布计量资料以均数 $\pm$ 标准差表示采用独立样本 t 检验。Logistic 回归分析双能 CT 参数与 NSCLC 患者发生纵膈淋巴结转移相关性,受试者工作特征曲线(Receiver operator characteristics curve, ROC)分析双能 CT 参数对 NSCLC 患者发生纵膈淋巴结转移的预测价值。所有统计均采用双侧检验,检验水准 $\alpha=0.05$ 。

2 结果

2.1 NSCLC 患者纵膈淋巴结转移和未转移患者双能 CT 参数比较

100 例患者均顺利完成肺癌根治手术和纵膈淋巴结清扫手术,可检测纵膈淋巴结 193 枚,经术后病理证实转移 91 枚,42 例(转移组),未转移 102 枚,58 例(未转移组)。转移组 λ HU、斜率比值、IC、NIC 均低于未转移组($P<0.05$),WC、NWC 与对照组比较无统计学差异($P>0.05$),见表 1。

表 1 转移组和未转移组 λ HU、斜率比值、IC、WC、NIC、NWC 比值比较($\bar{x}\pm s$)

Table 1 Comparison of λ HU, slope ratio, IC, WC, NIC, NWC ratio between metastatic group and non-metastatic group($\bar{x}\pm s$)

Groups	n	λ HU	Slope ratio	IC(100 μ g/cm ³)	WC(mg/cm ³)	NIC	NWC
Metastatic group	42	1.03 $\pm$ 0.29	0.97 $\pm$ 0.25	24.61 $\pm$ 3.12	1025.35 $\pm$ 26.35	0.41 $\pm$ 0.13	1.01 $\pm$ 0.02
Non-metastatic group	58	1.56 $\pm$ 0.51	1.42 $\pm$ 0.43	30.32 $\pm$ 4.51	1029.35 $\pm$ 26.04	0.55 $\pm$ 0.21	1.00 $\pm$ 0.03
t		6.058	6.074	7.067	0.754	3.820	1.878
P		0.000	0.000	0.000	0.452	0.000	0.063

2.2 转移组淋巴结与原发病灶双能 CT 参数比较

转移组 λ HU、IC、WC、NIC、NWC 与原发病灶比较均无统

计学差异($P>0.05$),见表 2。

表 2 转移组淋巴结与原发病灶 λ HU、IC、WC、NIC、NWC 比值比较($\bar{x} \pm s$)Table 2 Comparison of λ Hu, IC, WC, NIC, NWC ratio between lymph nodes and primary lesions in metastatic group($\bar{x} \pm s$)

Groups	n	λ HU	IC(100 $\mu\text{g}/\text{cm}^3$)	WC(mg/cm^3)	NIC	NWC
Metastatic group	42	1.03 $\pm$ 0.29	24.61 $\pm$ 3.12	1025.35 $\pm$ 26.35	0.41 $\pm$ 0.13	1.01 $\pm$ 0.02
Primary lesions	42	1.10 $\pm$ 0.31	25.43 $\pm$ 3.61	1024.49 $\pm$ 26.32	0.39 $\pm$ 0.12	1.02 $\pm$ 0.03
t		1.069	1.114	0.150	0.733	1.797
P		0.288	0.269	0.881	0.466	0.076

2.3 未转移组淋巴结与原发病灶双能 CT 参数比较

NWC 与原发病灶比较无统计学差异($P>0.05$),见表 3。未转移组 λ HU、IC、NIC 高于原发病灶 ($P<0.05$),WC、表 3 未转移组淋巴结与原发病灶 λ HU、IC、WC、NIC、NWC 比值比较($\bar{x} \pm s$)Table 3 Comparison of λ Hu, IC, WC, NIC, NWC ratio between lymph nodes and primary lesions in non-metastatic($\bar{x} \pm s$)

Groups	n	λ HU	IC(100 $\mu\text{g}/\text{cm}^3$)	WC(mg/cm^3)	NIC	NWC
Non-metastatic group	58	1.56 $\pm$ 0.51	30.32 $\pm$ 4.51	1029.35 $\pm$ 26.04	0.55 $\pm$ 0.21	1.00 $\pm$ 0.03
Primary lesions	58	1.13 $\pm$ 0.36	22.51 $\pm$ 3.06	1025.16 $\pm$ 24.72	0.31 $\pm$ 0.11	1.01 $\pm$ 0.02
t		5.246	10.913	0.889	7.710	1.690
P		0.000	0.000	0.376	0.000	0.094

2.4 双能 CT 参数与 NSCLC 纵膈淋巴结转移的 Logistic 回归分析

因变量,建立 Logistic 回归方程,结果 λ HU、斜率比值、IC、NIC 均与纵膈淋巴结转移有关($P<0.05$),见表 4。以 λ HU、斜率比值、IC、NIC 为自变量,纵膈淋巴结转移为

表 4 Logistic 回归分析结果

Table 4 Logistic regression analysis results

Factors	β	SE	Wald χ^2	OR(95%CI)	P
λ HU	-0.623	0.203	9.419	0.536(0.025~0.792)	0.003
Slope ratio	-0.529	0.165	10.279	0.589(0.031~0.828)	0.005
IC	-0.732	0.185	15.656	0.481(0.106~0.974)	0.000
NIC	-0.859	0.211	16.574	0.424(0.165~0.942)	0.000

2.5 双能 CT 参数诊断 NSCLC 纵膈淋巴结转移的效能分析

ROC 分析 λ HU、斜率比值、IC、NIC 诊断 NSCLC 纵膈淋巴结转移的曲线下面积(Area under the curve, AUC)分别为 0.849 (95%CI: 0.775~0.923, $P=0.000$)、0.871 (95%CI: 0.799~0.943,

$P=0.000$)、0.838 (95% CI: 0.760~0.917, $P=0.000$)、0.860 (95% CI: 0.786~0.934, $P=0.000$),见图 1。 λ HU、斜率比值、IC、NIC 诊断 NSCLC 纵膈淋巴结转移的灵敏度、特异度、阳性预测值、阴性预测值见表 5。

表 5 λ HU、斜率比值、IC、NIC 诊断 NSCLC 纵膈淋巴结转移的效能分析Table 5 The efficacy analysis of λ Hu, slope ratio, IC, NIC in diagnosis of mediastinal lymph node metastasis in NSCLC

Indexes	Cut-off	Sensitivity(%)	Specificity(%)	Positive predictive value(%)	Negative predictive value(%)
λ HU	1.31	80.95	79.31	73.91	85.19
NIC	0.43	85.71	84.48	80.00	83.64
IC	25.34(100 $\mu\text{g}/\text{cm}^3$)	78.57	81.03	75.00	83.92
Slope ratio	1.13	83.33	82.76	77.78	87.27

3 讨论

NSCLC 早期诊断率低,仅 20%患者可在疾病早期得到有效手术切除,约 50%患者生存状况较差^[10]。对 NSCLC 患者进行准确病理分期可为治疗策略制定提供可靠依据^[11],进而改善预

后。其中对淋巴结转移的准确评估关系临床治疗策略的调整,未发生纵膈转移患者,手术根治性切除是唯一有效的方法,而伴纵膈淋巴结转移患者需术前进行联合放化疗等治疗。因此,寻找能精确判断 NSCLC 淋巴结转移的非侵入性诊断方法,对治疗方案选择、危险分层、疗效评估、预后预测均有重要意义。

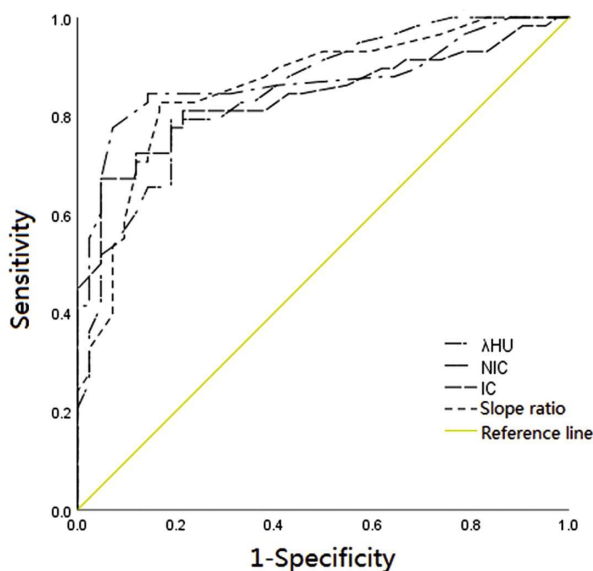


图1 λ HU、斜率比值、IC、NIC 诊断 NSCLC 纵膈淋巴结转移的 ROC 图
Fig.1 The ROC of λ Hu, slope ratio, IC, NIC in diagnosis of mediastinal lymph node metastasis in NSCLC

纵膈淋巴结是 NSCLC 常见转移部位,纵膈淋巴结是否转移、转移数量、区域与手术方式、切除范围、术后复发等均密切相关^[12,13]。目前临床诊断纵膈淋巴结转移的方法有 X 线片、MRI、CT、支气管镜、纵膈镜、胸腔镜等,随着 CT 技术的快速发展,逐渐成为无创诊断 NSCLC 病理分期的影像学手段。常规 CT 对淋巴结转移价值有限,双能量增强 CT 快速 kVp 交换技术可产生两个一致的能量数据集,基于投影重建和线性衰减系数生成不同 CT 值下单能量图像,提供不同组织定量信息^[14]。与常规 CT 相比,双能量增强 CT 弥补了常规 CT 诊断的单一参数弊端,其定量分析技术和多参数图像为多系统疾病诊断提供更可靠的依据^[15-17]。双能量增强 CT 在良恶性肺结节鉴别诊断、淋巴结转移、组织学分型方面均优于常规 CT^[18]。

CT 值反映物质对 X 线衰减能力,常规 CT 无法准确反映物质对 X 线衰减特征,双能量增强 CT 不受混合能量成像形成的硬化伪影的影响,测量 CT 值更为准确和稳定,因此能更好反映组织特性。本研究转移组纵膈淋巴结 λ HU 低于未转移组,与邝平定^[9]报道结果一致,分析原因为肿瘤侵犯纵膈淋巴结,代替淋巴结正常免疫细胞,引起淋巴结成分变化以及周围环境改变,导致对 X 线衰减能力变化,出现 CT 值差异^[19,20]。碘原子序数高于体内软组织,双能量增强 CT 利用这一特性可区分碘与软组织生成碘基物质浓度图,观察碘在体内组织分布情况,反映组织血流灌注水平^[21,22]。本研究发现转移组 IC、NIC 低于未转移组,崔元龙^[3]同样发现 NSCLC 纵膈淋巴结转移患者动脉期、静脉期 NIC 均低于未转移患者,Sato K^[23]采用双能量增强 CT 判断直肠癌直肠旁淋巴结和盆腔外侧淋巴结是否发生转移,发现发生转移患者 NIC 低于未转移患者。分析原因为癌细胞淋巴结转移可引起淋巴结发生不同程度坏死,淋巴结血管数量减少,进入转移性淋巴结血流量降低,导致对比剂进入淋巴结剂量较正常淋巴结低^[24]。本研究转移组 λ HU、IC、NIC 与原发病灶比较无统计学差异,而未转移组 λ HU、IC、NIC 则明显高于原发病灶,分析原因为发生转移的纵膈淋巴结与肺癌原发病灶血供、细胞成分相似,因此其 CT 值变化的能谱谱线相似,组织灌

注相似,未转移淋巴结多为炎性结节,细胞成分与原发病灶迥异,因此能谱曲线图不同,组织血流灌注参数不同。提示转移淋巴结与原发病灶具有同源性^[25-27]。

本研究采用 Logistic 回归分析 λ HU、斜率比值、IC、NIC 均与 NSCLC 纵膈淋巴结转移存在密切关系,其中 λ HU、斜率比值、IC、NIC 均与纵膈淋巴结转移呈负相关,提示 λ HU、斜率比值、IC、NIC 降低预示着更大的淋巴结转移风险,说明 λ HU、斜率比值、IC、NIC 对 NSCLC 纵膈淋巴结转移存在一定预测价值。进一步 ROC 分析发现 λ HU、斜率比值、IC、NIC 诊断 NSCLC 纵膈淋巴结转移的 AUC 分别为 0.849、0.871、0.838、0.860,灵敏度分别为 80.95%、85.71%、78.57%、83.33%,特异度分别为 79.31%、84.48%、81.03%、82.76%,Zhao Y^[20] 研究显示 IC、NIC、 λ HU 诊断甲状腺颈部淋巴结转移的敏感性分别为 83.3%、96.1%、88.2%,特异性分别为 91.2%、76.5%、82.4%,准确率分别为 85.3%、91.2%、86.8%。提示双能量增强 CT 对 NSCLC 纵膈淋巴结转移具有较高诊断价值,可弥补 CT 形态学诊断的弊端,更准确地为 NSCLC 淋巴结转移提供参考^[28-30]。

综上,NSCLC 纵膈转移淋巴结双能量增强 CT 参数与原发病灶具有相似性,与未转移淋巴结有明显差异性,双能量增强 CT 扫描对 NSCLC 纵膈淋巴结转移具有一定诊断价值,可为临床治疗提供更可靠的信息和依据。

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