甲状腺癌伴肺转移患者总体生存率和癌症特异性生存率的Nomogram模型建立及验证

欧振飞, 齐齐, 郭孝兹, 张雪娟

青岛大学附属医院, 山东 青岛
Email: ‘dzhangxue@126.com

摘要：目的: 本研究的目的是开发一种有效的Nomogram来识别和预测甲状腺癌伴肺转移(thyroid cancer lung metastasis)患者，预测TCLM患者的总生存期(overall survival)和癌症特异性生存期(cancer specific survival)，从而协助临床诊断和治疗。方法: 本研究从SEER数据库共纳入544名已知甲状腺癌伴肺部转移的患者，并随机分配到训练组和验证组。采用Logistic回归筛选变量，并建立Nomogram模型。经过统计学分析我们发现年龄、组织学类型、肿瘤等级、肿瘤大小、肝转移、放疗、手术是构建Nomogram的重要变量。结果: 用于识别和预测TCLM患者OS和CSS的Nomogram模型在校准曲线和受试者工作特征曲线(ROC)上得到了很好的检验。结论: 本研究首先建立并验证TCLM患者预后相关的Nomogram模型，其中诊断年龄、组织学类型、肿瘤等级、肿瘤大小、肝转移、放疗、手术是影响该病预后的独立危险因素，帮助TCLM患者临床治疗及治疗后随访提供科学依据。

关键词：甲状腺癌，肺部转移，临床预后，Nomogram

A Nomogram for Distinction and Potential Prediction of Lung Metastasis in Thyroid Cancer Patients

Zhenfei Ou, Qi Qi, Xiaoci Guo, Xuejuan Zhang

Department of General Practice, Affiliated Hospital of Qingdao University, Qingdao Shandong
Email: ‘dzhangxue@126.com

Received: Jul. 26th, 2021; accepted: Aug. 24th, 2021; published: Aug. 31st, 2021

*通讯作者。
Abstract

Objective: The prognosis of thyroid cancer with lung metastasis is poor. Our aim is to develop a reliable tool to identify and predict lung metastasis (LM) in patients with thyroid cancer (TC), thereby assisting in clinical diagnosis and treatment. The aim of this study was to establish an effective Nomogram method for predicting overall survival (OS) and cancer specific survival (CSS) in TC patients with LM. Methods: A total of 544 patients with known distant metastatic status and epidemiological variables from the SEER database were enrolled and assigned randomly to training and validating groups in this study. Logistic regression was used to screen variables and a Nomogram was established. After multivariate logistic regression, age, histologic type, grade, tumor size, liver metastasis, radiotherapy and surgery were the important variables to construct the Nomogram. Results: The Nomogram used to identify and predict the OS and CSS in TCLM patients passed the calibration and validation steps. The calibration curve and receiver operating characteristic curves (ROC) indicated the good performance of the Nomogram. Conclusions: Our Nomogram is a reliable and robust tool for the identification and prediction of LM in TC patients, thus helping to better select medical examinations and optimize treatment in collaboration with medical oncologists and surgeons.

Keywords

Thyroid Cancer, Lung Metastasis, Prognosis, Nomogram
年间，共发现 544 例符合研究条件的患者，并建立了 Nomogram 模型。患者被随机分为训练组(70%)和验证组(30%)。在本研究中，训练组患者用于制定 Nomogram 模型，验证组患者用于验证模型。

数据收集
本研究采用 15 个变量来确定 TCLM 患者的预后因素，包括年龄、性别、种族、等级、组织学类型、对一侧的偏重、肿瘤大小、T 期、N 期、手术、化疗、放疗、肝转移、骨转移和脑转移。CSS 是指从诊断日到因癌症死亡之日的时间间隔。组织学亚型分为四类，IDO~O~3 编码如下：甲状腺乳头状癌(PTC)：8340.8341.8342.8344.8260；甲状腺滤泡状癌(FTC)：8330.8331.8335；甲状腺瘤(ATC)：8020.8021.8030.8032；甲状腺髓样癌(MTC)：8510。

统计分析
在总共 544 例符合条件的 TCLM 患者中，374 例被随机分配到训练队列，其余 170 例患者被分配到验证队列，以构建和验证 Nomogram 模型。本研究中所有统计分析均采用 SPSS 25.0 和 R 软件 (3.6.1 版) 进行。采用 chi-square 检验来比较训练队列和测试队列之间的变量。在本研究中，P 值 < 0.05 (两边) 认为具有统计学意义。应用单变量 logistic 分析来确定 LM 相关因素。对于预后因素，应用单变量 Cox 回归分析来确定预后变量。然后将单变量 Cox 回归分析中的重要变量纳入多变量 Cox 回归分析，确定 TCLM 的独立预后因素。OS 和 CSS 被指定为本研究的两个终点。总生存率：因任何原因死亡的病人作为总体死亡病例组，其诊断为 TCLM 到其死亡的时间作为衡量总体生存率的标准。在最后一次随访中仍存活的病人作为总体死亡病例组的对照观察组。肿瘤特异性生存率：因 TCLM 死亡的病人作为肿瘤相关特异性死亡病例组，其诊断为 TCLM 到其死亡的时间作为衡量肿瘤特异性生存率的标准。在最后一次随访中仍存活的病人或者不是因 TCLM 死亡的病人作为对照观察组。

根据确定的独立预后因素，通过 R 软件中的 RMS 包分别建立 3 年、5 年 OS 和 CSS 的 Nomogram 模型。同时，生成预测 Nomogram 模型的受试者工作特征曲线(ROC)曲线[8]。用曲线下面积(AUC)来评价模型的预测能力。如果 AUC 在 0.5~1 之间，则认为该模型良好。如果 AUC > 0.75，则认为该模型表现出色[9]。此外还建立了 Nomogram 模型的校准曲线[10]。

3. 结果

人口信息
所有纳入的 TC 患者在初诊时均被确认伴有肺转移。表 1 显示了所有患者的一般资料。患者按年龄被分为两组(20~58 岁和 59~90 岁)。285 名患者(52.39%)为女性，其余 259 名(47.61%)为男性。在入选患者的种族方面，主要是白人(n = 428 [78.68%])。在各种组织学亚型中，PTC (n = 316 [58.09%])是最常见的亚型。最常见的 T 期和 N 期分别为 T3、4 期(85.48%)和 N0 期(64.89%)。其中骨转移 87 例(15.99%)，脑转移 17 例(3.13%)，肝转移 23 例(4.23%)。此外，数据还强调手术和放疗是患者最广泛接受的治疗方式(分别为 n = 397 [72.98%]和 n = 335 [61.58%])，而化疗则为少数病例(n = 112 [20.59%])。

| 变量   | 总队列(N = 544) | 建模队列(N = 374) | 验证队列(N = 170) |
|--------|----------------|------------------|------------------|
| 年龄   | n              | %                | n                | %                |
| 20~59  | 165            | 30.33%           | 116              | 31.02%           | 49               | 28.82%           |
| 60~90  | 379            | 69.67%           | 258              | 68.98%           | 121              | 71.18%           |
| 差异 | 女  | 52.39% | 197 | 52.67% | 88  | 51.76% |
|------|-----|--------|-----|--------|-----|--------|
|      | 男  | 47.61% | 177 | 47.33% | 82  | 48.24% |
| 种族 |     |        |     |        |     |        |
| 白人 | 428 | 78.68% | 294 | 78.61% | 134 | 78.82% |
| 黑人 | 49  | 9.01%  | 33  | 8.82%  | 16  | 9.41%  |
| 其他 | 77  | 14.15% | 47  | 12.57% | 30  | 17.65% |
| 组织学类型 |     |        |     |        |     |        |
| 乳头状癌 | 316 | 58.09% | 210 | 56.15% | 106 | 62.35% |
| 滤泡癌 | 65  | 11.95% | 52  | 13.90% | 13  | 7.65%  |
| 未分化癌 | 136 | 25.00% | 90  | 24.06% | 46  | 27.06% |
| 腺样癌 | 27  | 4.96%  | 22  | 5.88%  | 5   | 2.94%  |
| 等级 |     |        |     |        |     |        |
| 低(I, II) | 90  | 16.54% | 61  | 16.31% | 29  | 17.06% |
| 高(III, IV) | 206 | 37.87% | 142 | 37.97% | 64  | 37.65% |
| 不确定 | 248 | 45.59% | 171 | 45.72% | 77  | 45.29% |
| 位置 |     |        |     |        |     |        |
| 左侧为主 | 17  | 3.13%  | 13  | 3.48%  | 4   | 2.35%  |
| 右侧为主 | 20  | 3.68%  | 12  | 3.21%  | 8   | 4.71%  |
| 双侧 | 5   | 0.92%  | 3   | 0.80%  | 2   | 1.18%  |
| 不对称 | 502 | 92.28% | 346 | 92.51% | 156 | 91.76% |
| 肿瘤大小 |     |        |     |        |     |        |
| 3~80 | 464 | 85.29% | 318 | 85.03% | 146 | 85.88% |
| 81~160 | 80  | 14.71% | 56  | 14.97% | 24  | 14.12% |
| T |     |        |     |        |     |        |
| T1~2 | 79  | 14.52% | 45  | 12.03% | 34  | 20.00% |
| T3~4 | 465 | 85.48% | 329 | 87.97% | 136 | 80.00% |
| N |     |        |     |        |     |        |
| N0 | 191 | 35.11% | 132 | 35.29% | 59  | 34.71% |
| N1 | 353 | 64.89% | 242 | 64.71% | 111 | 65.29% |
| 骨转移 |     |        |     |        |     |        |
| No | 425 | 78.13% | 283 | 75.67% | 142 | 83.53% |
| Yes | 87  | 15.99% | 86  | 22.99% | 1   | 0.59%  |
| 不确定 | 32  | 5.88%  | 5   | 1.34%  | 27  | 15.88% |
| 脑转移 |     |        |     |        |     |        |
| No | 511 | 93.93% | 350 | 93.58% | 161 | 94.71% |
| Yes | 17  | 3.13%  | 15  | 4.01%  | 2   | 1.18%  |
Continued

| 不确定 | 16 | 2.94% | 9 | 2.41% | 7 | 4.12% |
| 肝转移 | | | | | | |
| No | 505 | 92.83% | 346 | 92.51% | 159 | 93.53% |
| Yes | 23 | 4.23% | 22 | 5.88% | 1 | 0.59% |
| 不确定 | 16 | 2.94% | 6 | 1.60% | 10 | 5.88% |
| 化疗 | | | | | | |
| no/Unknown | 432 | 79.41% | 298 | 79.68% | 134 | 78.82% |
| yes | 112 | 20.59% | 76 | 20.32% | 36 | 21.18% |
| 放疗 | | | | | | |
| no/Unknown | 199 | 36.58% | 146 | 39.04% | 53 | 31.18% |
| yes | 335 | 61.58% | 228 | 60.96% | 107 | 62.94% |

OS 和 CSS 的预后因素

表 2 显示了基于 OS 的单变量和多变量 Cox 回归分析。统计学评价显示年龄(P = 0.003)、组织学类型(P = 0.001)、等级(P < 0.001)、肿瘤大小(P = 0.002)、T 期(P = 0.128)、合并肝转移(P = 0.037)放射治疗(P < 0.001)和手术(P < 0.001)为独立危险因素。表 3 显示了基于 CCS 的单变量和多变量 Cox 回归分析。发现年龄(P = 0.001)、等级(P = 0.009)、合并肝转移(P = 0.001)、组织学亚型(P = 0.003)和放射治疗(P = 0.001)是独立的危险因素。统计学评价显示，年龄(P = 0.032)、组织学类型(P = 0.012)、等级(P = 0.001)、肿瘤大小(P = 0.001)、T 期(P = 0.153)、合并肝转移(P = 0.016)放射治疗(P = 0.001)和手术(P < 0.001)为独立危险因素。

| 表 2. Overall survival rate in univariate and multivariate Cox regression analyses of the modeling group cohort | 表 2. 单变量和多变量 Cox 回归分析建模组队列中的总体存活率。 |
|---|---|
| | HR (95% CI) | p | HR (95% CI) | p |
| 年龄 | | | | |
| 20–59 | Reference | | Reference | |
| 60–90 | 1.957 | 1.421–2.696 | <0.001 | 1.629 | 1.175–2.257 | 0.003 |
| 性别 | | | | |
| 女 | Reference | | | |
| 男 | 1.122 | 0.861–1.462 | 0.394 | |
| 种族 | | | | |
| 白人 | Reference | | | |
| 黑人 | 0.569 | 0.309–1.046 | 0.07 | |
| 其他 | 1.075 | 0.730–1.583 | 0.714 | |
| 组织学类型 | | | | |
| 乳头状癌 | Reference | | Reference | |
| 滤泡癌 | 0.946 | 0.601–1.491 | 0.812 | 0.58 | 0.352–0.955 | 0.032 |
| 未分化癌 | 10.151 | 7.266–14.184 | <0.001 | 2.611 | 1.608–4.239 | 0.001 |
| 髓样癌 | 1.769 | 0.988–3.167 | 0.055 | 0.836 | 0.434–1.610 | 0.592 |
### Continued

| 等级 | 参考 | P值 | 参考 |
|------|------|------|------|
| 低 (I, II) | Reference | <0.001 | Reference |
| 高 (III, IV) | 7.17 | 4.436–11.588 | 3.383 | 1.909–5.994 | <0.001 |
| 不确定 | 1.397 | 0.853–2.288 | 0.185 | 1.099 | 0.662–1.827 | 0.714 |
| 位置 | | | | |
| 左侧为主 | | Reference |
| 右侧为主 | 0.927 | 0.377–2.284 | 0.87 |
| 双侧 | 0.95 | 0.208–4.340 | 0.947 |
| 不对称 | 0.661 | 0.349–1.249 | 0.202 |
| 肿瘤大小 | | | | |
| 3–80 | | Reference |
| 81–160 | 2.423 | 1.736–3.381 | <0.001 |
| T | | | | |
| T1–2 | | Reference |
| T3–4 | 2.482 | 1.469–4.195 | 0.001 |
| N | | | | |
| N0 | | Reference |
| N1 | 1.303 | 0.981–1.731 | 0.068 |
| 骨转移 | | | | |
| no | | Reference |
| yes | 1.228 | 0.901–1.675 | 0.194 |
| 不确定 | 1.556 | 0.576–4.199 | 0.383 |
| 脑转移 | | | | |
| no | | Reference |
| yes | 1.444 | 0.786–2.652 | 0.237 |
| 不确定 | 1.482 | 0.697–3.150 | 0.306 |
| 肝转移 | | | | |
| no | | Reference |
| yes | 2.17 | 1.350–3.487 | 0.001 |
| 不确定 | 1.075 | 0.399–2.896 | 0.886 |
| 化疗 | | | | |
| no/Unknown | | Reference | Reference |
| yes | 2.527 | 1.873–3.411 | <0.001 |
| 放疗 | | | | |
| no/Unknown | | Reference | Reference |
| yes | 0.453 | 0.347–0.591 | <0.001 |
| 手术 | | | | |
| no/Unknown | | Reference | Reference |
| yes | 0.243 | 0.184–0.321 | <0.001 |

DOI: 10.12677/acm.2021.118561 3825
### Table 3. Univariate and multivariate Cox regression analyses of tumor-specific survival rates in the cohort of modelers.

表3. 单变量和多变量Cox回归分析建模组队列中的肿瘤特异性存活率。

|                | HR     | (95% CI)       | p     | HR     | (95% CI)       | P     |
|----------------|--------|----------------|-------|--------|----------------|-------|
| 年龄            |        |                |       |        |                |       |
| 20~59          | Reference |                |       | 2.864  | 1.311~1.651    | 0.001 |
| 60~90          | 1.864  | 1.311~2.651    | 0.001 | 1.489  | 1.035~2.142    | 0.032 |
| 性别            |        |                |       |        |                |       |
| 女             | Reference |                |       |        |                |       |
| 男             | 1.147  | 0.848~1.552    | 0.372 |        |                |       |
| 种族            |        |                |       |        |                |       |
| 白人           | Reference |                |       |        |                |       |
| 黑人           | 0.466  | 0.218~0.997    | 0.049 | 0.813  | 0.374~1.769    | 0.602 |
| 其他           | 1.23   | 0.808~1.872    | 0.334 | 1.317  | 0.845~2.051    | 0.223 |
| 组织学类型      |        |                |       |        |                |       |
| 乳头状癌       | Reference |                |       |        |                |       |
| 滤泡癌         | 0.984  | 0.594~1.629    | 0.949 | 0.483  | 0.273~0.854    | 0.012 |
| 未分化癌       | 9.776  | 6.848~14.538   | <0.001| 2.368  | 1.370~4.094    | 0.002 |
| 髓样癌         | 1.794  | 0.924~3.481    | 0.084 | 0.696  | 0.317~1.528    | 0.367 |
| 等级            |        |                |       |        |                |       |
| Low (I, II)    | Reference |                |       |        |                |       |
| High (III, IV) | 7.98   | 4.518~14.093   | <0.001| 3.792  | 1.912~7.524    | 0.001 |
| 不确定         | 1.591  | 0.887~2.852    | 0.119 | 1.196  | 0.650~2.201    | 0.564 |
| 位置            |        |                |       |        |                |       |
| 左侧为主       | Reference |                |       |        |                |       |
| 右侧为主       | 0.551  | 0.174~1.744    | 0.31  |        |                |       |
| 双侧           | 0.643  | 0.124~3.328    | 0.598 |        |                |       |
| 不对称         | 0.422  | 0.172~1.037    | 0.06  |        |                |       |
| 肿瘤大小       |        |                |       |        |                |       |
| 3~80           | Reference |                |       |        |                |       |
| 81~160         | 2.624  | 1.823~3.778    | <0.001| 2.076  | 1.348~3.196    | 0.001 |
| T              |        |                |       |        |                |       |
| T1~2           | Reference |                |       |        |                |       |
| T3~4           | 2.325  | 1.261~4.285    | 0.001 | 1.637  | 0.832~3.220    | 0.153 |
| N s            |        |                |       |        |                |       |
| N0             | Reference |                |       |        |                |       |
| N1             | 1.377  | 0.989~1.917    | 0.058 |        |                |       |
| 骨转移         |        |                |       |        |                |       |
| no             | Reference |                |       |        |                |       |
| yes            | 1.242  | 0.880~1.753    | 0.217 |        |                |       |
| 不确定         | 1.635  | 0.603~4.431    | 0.334 |        |                |       |

DOI: 10.12677/acm.2021.118561 3826
构建 Nomogram 模型

根据单变量和多变量的 Cox 回归结果，构建 3 年和 5 年 OS 和 CSS 预后模型(图 1)。
Figure 1. Nomograms predict 3- and 5-year OS (a) and CSS (b)

图 1. Nomograms 预测 3 年和 5 年 OS (a) 和 CSS (b)

校准曲线显示，TCLM 患者的预测结果与实际生存率之间具有很好的一致性（图 2、图 3）。ROC 分析显示，训练队列中 3 年、5 年 OS 的 AUC 分别为 0.805、0.786，验证队列中为 0.868、0.89（图 4）。同样的在 CSS 的训练队列中 AUC 分别为 0.817 和 0.791，在验证队列中分别为 0.882 和 0.935（图 5）。
Figure 2. OS calibration curves of the training cohort for 3 years (a) and 5 years (b) and validation cohort for 3 years (c) and 5 years (d)

图2. 训练队列3年(a)和5年(b) OS 校准曲线，验证队列3年(c)和5年(d) OS 校准曲线
Figure 3. CCS calibration curves of the training cohort at 3 years (a) and 5 years (b), and the validation cohort at 3 years (c) and 5 years (d).

图 3. 训练队列 3 年 (a) 和 5 年 (b) CCS 校准曲线，验证队列 3 年 (c) 和 5 年 (d) CCS 校准曲线

Figure 4. ROC curves of 3-year (a) and 5-year (b) OS in the training cohort; Verify the ROC curves for 3-year (c) and 5-year (d) OS in the queue.

图 4. 训练队列 3 年 (a)、5 年 (b) OS 的 ROC 曲线；验证队列 3 年 (c)、5 年 (d) OS 的 ROC 曲线
图5. 训练队列中3年(a)、5年(b) CCS的ROC曲线；验证队列中3年(c)、5年(d) CCS的ROC曲线

4. 讨论

鉴于TC患者良好的可治疗性和生存率，在医学界它是一种相对良性的癌症[11]。在对1516例甲状腺乳头状癌的回顾性生存分析中，肺转移和多器官转移之间没有显示出差异。此外，对于一些临床特征，有报道称年龄、性别、术后甲状腺球蛋白(Tg)水平和肿瘤大小是TC患者引起肺转移的危险因素[12]。然而到目前为止，还没有建立相应的预测模型，这意味着无法通过综合所有独立的相关预测因子来确定TCLM的个体风险。

肺是分化型甲状腺癌(DTCs)最常见的转移部位，其次是骨骼，很少有脑和肝脏[13]。据报道，DTC
患者发生肺转移的10年生存率为25%~85%[14] [15]。虽然TCLM患者的预后极差，但早期发现对LMTC患者的预后至关重要。本研究通过基于大人群SEER数据库构建单变量和多变量Cox风险分析模型，进一步探讨TCLM患者预后的重要因素，并构建TCLM的CSS和OS相关Nomogram模型，以帮助识别高死亡风险患者，制定合适的治疗策略。在我们的研究结果显示，年龄、组织学类型、等级、肿瘤大小、肝转移、放疗、手术是TCLM患者OS或CSS的重要的预测因素。这些因素与TCLM患者之间的关系在以往的研究中已有报道。

Jianing Tang等人的研究认为，白人和黑人患者在TC的疾病特异性生存的危险因素上存在显著差异[16]。但在我们的分析中没有发现它是一个独立的预后因素。众所周知年龄是DTC复发和死亡率的预测因素[17]。我们研究证实年龄是一个重要预测因素。本研究发现肺转移的组织学类型也是一个重要的预后因素。我们研究结果显示，未分化的TCLM死亡风险明显高于其他组织学类型的患者。Hu P.等人[18]和Huang R.等人[19]的研究均表明，等级是恶性肿瘤的独立预测因素，同样我们的研究也发现是这样。以往的研究[20]报道了肿瘤大小级别与肿瘤生存率之间的关系，研究发现肿瘤直径较大的患者预后明显低于肿瘤直径较小的患者。在我们的研究中TCLM患者肿瘤大小≥81mm提示预后不良。

甲状腺癌肝转移相当少见，报道频率仅为0.5%[21] [22]。这些患者的治疗效果不佳，这是导致TC死亡的主要原因[23]。本研究中TCLM患者的OS和CSS显示，肝转移的存在是预后相关的独立危险因素。Chenyuan Li等人对SEER数据库的研究[24]提示放射性碘(RAI)治疗TC患者可改善年龄<45岁组和分化良好组的生存率。与我们的研究结果一致。放射性碘(RAI)治疗在TC的治疗中起着非常重要的作用[25]。

5.结论
总之，我们的研究是首次建立并验证了TCLM患者的预后Nomogram模型，该模型将为预测TCLM患者的3年、5年OS和CSS提供更全面、更准确的模型。此外Nomogram模型的建立将有助于识别高死亡风险的患者，帮助临床医生制定合适的治疗策略。

利益冲突
本人与其他作者宣称没有任何利益冲突，未接受任何不当的职务或财务利益。

作者贡献声明
欧振飞负责文章撰写；张雪娟负责总体修改；齐齐，郭孝兹参与数据处理等。

参考文献
[1] Siegel, R.L., Miller, K.D., Fuchs, H.E., et al. (2021) Cancer Statistics, 2021. CA: A Cancer Journal for Clinicians, 71, 7-33. https://doi.org/10.3322/caac.21654
[2] Hundahl, S.A., Fleming, I.D., Fremgen, A.M., et al. (1998) A National Cancer Data Base Report on 53,856 Cases of Thyroid Carcinoma Treated in the U.S., 1985-1995. Cancer, 83, 2638-2648. https://doi.org/10.1002/(SICI)1097-0142(19981215)83:12<2638::AID-CNCR31>3.0.CO;2-1
[3] Mazzaferri, E.L. and Kloos, R.T. (2001) Clinical Review 128: Current Approaches to Primary Therapy for Papillary and Follicular Thyroid Cancer. The Journal of Clinical Endocrinology and Metabolism, 86, 1447-1463. https://doi.org/10.1210/jcem.86.4.7407
[4] Huang, I.C., Chou, F.F., Liu, R.T., et al. (2012) Long-Term Outcomes of Distant Metastasis from Differentiated Thyroid Carcinoma. Clinical Endocrinology, 76, 439-447. https://doi.org/10.1111/j.1365-2265.2011.04231.x
[5] Balachandran, V.P., Gonen, M., Smith, J.J., et al. (2015) Nomograms in Oncology: More than Meets the Eye. The Lancet Oncology, 16, e173-e180. https://doi.org/10.1016/S1470-2045(14)71116-7
[6] Song, H.J., Qiu, Z.L., Shen, C.T., et al. (2015) Pulmonary Metastases in Differentiated Thyroid Cancer: Efficacy of Radioiodine Therapy and Prognostic Factors. European Journal of Endocrinology, 173, 399-408. https://doi.org/10.1530/EJE-15-0296

[7] Lin, Z., Yan, S., Zhang, J., et al. (2018) A Nomogram for Distinction and Potential Prediction of Liver Metastasis in Breast Cancer Patients. Journal of Cancer, 9, 2098-2106. https://doi.org/10.7150/jca.24445

[8] Heagerty, P.J., Lumley, T. and Pepe, M.S. (2000) Time-Dependent ROC Curves for Censored Survival Data and a Diagnostic Marker. Biometrics, 56, 337-344. https://doi.org/10.1111/j.0006-341X.2000.00337.x

[9] Uka, K., Chayama, K., Aikata, H., et al. (2007) Clinical Features and Prognosis of Patients with Extrahepatic Metastases from Hepatocellular Carcinoma. World Journal of Gastroenterology, 13, 414-420. https://doi.org/10.3748/wjg.v13.i3.414

[10] Vickers, A.J. and Elkin, E.B. (2006) Decision Curve Analysis: A Novel Method for Evaluating Prediction Models. Medical Decision Making, 26, 565-574. https://doi.org/10.1177/0272989X06295361

[11] Randle, R.W., Bushman, N.M., Orne, J., et al. (2017) Papillary Thyroid Cancer: The Good and Bad of the “Good Cancer”. Thyroid, 27, 902-907.

[12] Lin, J.D., Chao, T.C., Chou, S.C., et al. (2004) Papillary Thyroid Carcinomas with Lung Metastases. Thyroid, 14, 1091-1096. https://doi.org/10.1089/thy.2004.14.1091

[13] Nixon, I.J., Whitcher, M.M., Palmer, F.L., et al. (2012) The Impact of Distant Metastases at Presentation on Prognosis in Patients with Differentiated Carcinoma of the Thyroid Gland. Thyroid, 22, 884-889. https://doi.org/10.1089/thy.2011.0535

[14] Cho, S.W., Choi, H.S., Yeom, G.J., et al. (2014) Long-Term Prognosis of Differentiated Thyroid Cancer with Lung Metastasis in Korea and Its Prognostic Factors. Thyroid, 24, 277-286. https://doi.org/10.1089/thy.2012.0654

[15] Chopra, S., Garg, A., Ballal, S., et al. (2015) Lung Metastases from Differentiated Thyroid Carcinoma: Prognostic Factors Related to Remission and Disease-Free Survival. Clinical Endocrinology, 82, 445-452. https://doi.org/10.1111/cen.12558

[16] Tang, J., Kong, D., Cui, Q.X., et al. (2018) Racial Disparities of Differentiated Thyroid Carcinoma: Clinical Behavior, Treatments, and Long-Term Outcomes. World Journal of Surgical Oncology, 16, 45. https://doi.org/10.1186/s12957-018-1340-7

[17] Brierley, J., Tsang, R., Panzarella, T., et al. (2010) Prognostic Factors and the Effect of Treatment with Radioactive Iodine and External Beam Radiation on Patients with Differentiated Thyroid Cancer Seen at a Single Institution over 40 Years. Clinical Endocrinology, 63, 418-427. https://doi.org/10.1111/j.1365-2265.2005.02358.x

[18] Hu, P., Bai, J., Liu, M., et al. (2020) Trends of Incidence and Prognosis of Gastric Neuroendocrine Neoplasms: A Study Based on SEER and Our Multicenter Research. Gastric Cancer, 23, 591-599. https://doi.org/10.1007/s10120-020-01046-8

[19] Huang, R., Sun, Z., Zheng, H., et al. (2019) Identifying the Prognosis Factors and Predicting the Survival Probability in Patients with Non-Metastatic Chondrosarcoma from the SEER Database. Orthopaedic Surgery, 11, 801-810. https://doi.org/10.1111/os.12521

[20] Ito, Y., Fukushima, M., Kihara, M., et al. (2012) Investigation of the Prognosis of Patients with Papillary Thyroid Carcinoma by Tumor Size. Endocrine Journal, 59, 457-464. https://doi.org/10.1507/endocrj.EJ12-0013

[21] Salvatori, M., Perotti, G., Rufini, V., et al. (2004) Solitary Liver Metastasis from Hürthle Cell Thyroid Cancer: A Case Report and Review of the Literature. Journal of Endocrinological Investigation, 27, 52-56. https://doi.org/10.1007/BF03350911

[22] Song, H.J., Xue, Y.L., Qiu, Z.L., et al. (2012) Uncommon Metastases from Differentiated Thyroid Carcinoma. Hellenic Journal of Nuclear Medicine, 15, 233-240.

[23] Nakanishi, K., Kikumori, T., Miyajima, N., et al. (2018) Impact of Patient Age and Histological Type on Radioactive Iodine Avidity of Recurrent Lesions of Differentiated Thyroid Carcinoma. Clinical Nuclear Medicine, 43, 482-485. https://doi.org/10.1097/RLU.0000000000002078

[24] Li, C., Wu, Q. and Sun, S.R. (2020) Radioactive Iodine Therapy in Patients with Thyroid Carcinoma with Distant Metastases: A SEER-Based Study. Cancer Control, 27, 1-9. https://doi.org/10.1177/1073274820914661

[25] Haugen, B.R., Aleander, L.E.K., Bible, K.C., et al. (2015) 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid, 26, 1-133. https://doi.org/10.1089/thy.2015.0020

DOI: 10.12677/acs.2021.118561