

· 临床研究 ·

高血糖与老年结直肠癌患者临床病理特征及术后并发症分析

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【摘要】 **目的** 探讨高血糖与老年结直肠癌患者临床病理特征及术后并发症的关系。**方法** 回顾性分析2019年7月至2020年7月于徐州医科大学附属医院诊治的老年结直肠癌患者78例,根据血糖水平分为高血糖组(36例)和血糖正常组(42例)。比较2组临床资料、病理指标、肿瘤标志物水平及术后并发症情况。采用SPSS 24.0软件进行统计分析。根据数据类型,组间比较分别采用 χ^2 检验、 t 检验、Wilcoxon检验、Fisher精确概率法或者Kruskal-Wallis检验。**结果** 2组在体质量指数(body mass index, BMI)和首发症状方面比较,差异均有统计学意义(均 $P<0.05$);高血糖组结肠癌多位于左半结肠,血糖正常组结肠癌多位于右半结肠,差异有统计学意义($P<0.05$);高血糖组病理分期多位于Ⅲ、Ⅳ期,血糖正常组病理分期多位于Ⅱ、Ⅲ期,差异有统计学意义($P<0.05$);与血糖正常组相比较,高血糖组更易出现淋巴结转移($P<0.05$)。高血糖组术前癌胚抗原(CEA)水平、CA199水平高于血糖正常组,差异均有统计学意义(均 $P<0.05$);2组术前CA125水平、CA242水平、CA724水平、CA50水平比较,差异均无统计学意义(均 $P>0.05$)。2组术后CEA、CA125、CA199、CA242、CA724和CA50检测结果比较,差异均无统计学意义(均 $P>0.05$)。2组术前CA199在组内不同病理分期比较,差异均有统计学意义(均 $P<0.05$)。高血糖组术前CEA水平在不同病理分期比较,差异有统计学意义($P<0.05$);血糖正常组术前CEA水平不同病理分期比较,差异无统计学意义($P>0.05$)。高血糖组术后并发症发生率高于血糖正常组,差异有统计学意义[12例(33.4%) 和12例(28.7%), $P<0.05$]。**结论** 高血糖状态是老年结直肠癌的危险因素,在老年结直肠癌患者中进行控制血糖的宣教,可降低术后感染率。

【关键词】 老年人;高血糖;结直肠癌;病理特征;术后并发症

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Clinicopathological characteristics of hyperglycemic elderly patients with colorectal cancer and analysis on postoperative complications

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【Abstract】 **Objective** To study the relationship of hyperglycemia with clinical pathological features and postoperative complications of colorectal cancer in the elderly. **Methods** Clinical data of 78 elderly patients with colorectal cancer in the Affiliated Hospital of Xuzhou Medical University from July 2019 to July 2020 were retrospectively collected in this study. They were and divided into hyperglycemia group ($n=36$) and normal blood glucose group ($n=42$) according to blood glucose level. The clinical data, pathological indexes, tumor markers and postoperative complications were compared between the 2 groups. SPSS statistics 24.0 was used for statistical analysis. Data comparison between 2 groups was performed using *Chi-square* test, student's *t* test, Wilcoxon test, Fisher exact probability test or Kruskal-Wallis test depending on date types. **Results** There were significant differences in body mass index (BMI) and first symptoms between the 2 groups (both $P<0.05$). In the hyperglycemia group, tumor masses were mostly located in the left colon, while in the normal glucose group, majorly in the right colon, and statistical difference was seen in the site ($P<0.05$). The tumor stage of the hyperglycemia group was generally in stage Ⅲ and Ⅳ, that of normal glucose group was in stage Ⅱ and Ⅲ ($P<0.05$), but lymph node metastasis was quite common in the former group ($P<0.05$). The hyperglycemia group had significantly higher preoperative levels of carcinoembryonic antigen (CEA) and CA199 when compared with the normal glucose group ($P<0.05$), but no

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such differences were observed in the preoperative levels of CA125, CA242, CA724 and CA50 and postoperative levels of CEA, CA125, CA199, CA242, CA724 and CA50 between the 2 groups (all $P>0.05$). The preoperative CEA level differed in different pathological stages ($P<0.05$), but such difference was only observed in the hyperglycemia group ($P<0.05$), not in the normal glucose group ($P>0.05$). The hyperglycemia group had notably higher incidence rate of postoperative complications than the other group [33.4% (12 cases) vs 28.7% (12 case), $P<0.05$]. **Conclusion** Hyperglycemia is a risk factor for colorectal cancer in the elderly. Health education on blood glucose control can reduce the postoperative infection rate in these patients.

【Key words】 aged; hyperglycemia; colorectal cancer; pathological features; postoperative complications

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在全球恶性肿瘤中,结直肠癌发病率位居第三,死亡率位居第二^[1],而老年人是结直肠癌高发人群^[2]。由于现代人饮食热量高、体力活动缺乏和中心性肥胖发生率增多,糖代谢异常的发病率在逐年上升。国外有学者发现,高血糖者罹患恶性肿瘤的风险较血糖正常者平均增加了20%~30%^[3],高糖水平能够促进肿瘤细胞增殖、侵袭和迁移、诱导凋亡抵抗,加速肿瘤的发生发展^[4]。我们旨在分析老年结直肠癌临床资料、病理特点、相关肿瘤标志物水平和术后并发症,探讨高血糖与老年结直肠癌临床病理特征及术后并发症的关系。

1 资料与方法

1.1 研究对象

回顾性分析2019年7月至2020年7月于徐州医科大学附属医院诊治的老年结直肠癌患者78例,根据血糖水平,分为高血糖组(36例)和血糖正常组(42例)。纳入标准:(1)病理确诊为结直肠癌;(2)均行手术治疗;(3)年龄 ≥ 60 岁;(4)病史及病理资料齐全。排除标准:(1)家族性结肠息肉病;(2)肛管鳞癌;(3)2个及以上原发肿瘤;(4)术前或术后行放化疗的结直肠癌;(5)伴有严重心脑血管疾病及多器官功能衰竭。术后1个月第1次复查的检测结果为术后肿瘤标志物水平。

1.2 方法

通过搜索电子病历系统,记录2组患者性别、年龄、手术记录、住院天数、病理资料、血糖情况及术前术后相关肿瘤标志物水平等,随访术后并发症,如手术切口感染、肺部感染、吻合口瘘、肠梗阻、尿潴留、深静脉血栓形成及伤口裂开情况。

1.3 统计学处理

采用SPSS 24.0软件进行统计分析。符合正态分布的计量资料用均数 \pm 标准差($\bar{x}\pm s$)表示,采用 t 检验;非正态分布的计量资料,用中位数和四分位数间距 $[M(Q_1, Q_3)]$ 表示,采用Wilcoxon检验。计数资料用例数(百分率)表示,采用 χ^2 检验或Fisher精

确概率法。不同病理分期CA199、癌胚抗原(carcino-embryonic antigen, CEA)的比较采用Kruskal-Wallis检验。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 2组患者临床资料比较

2组患者在性别、年龄、吸烟、饮酒、基础病、住院时间、手术时间及术中出血量情况比较,差异均无统计学意义(均 $P>0.05$);在体质指数(body mass index, BMI)和首发症状方面比较,差异均有统计学意义(均 $P<0.05$)。见表1。

2.2 2组患者病理特征比较

高血糖组结肠癌多位于左半结肠,血糖正常组结肠癌多位于右半结肠,差异有统计学意义($P<0.05$);高血糖组病理分期多位于Ⅲ、Ⅳ期,血糖正常组病理分期多位于Ⅱ、Ⅲ期,差异有统计学意义($P<0.05$);与血糖正常组相比较,高血糖组更易出现淋巴结转移($P<0.05$);2组直肠癌、组织类型、分化程度、肿瘤大小及大体形态比较,差异均无统计学意义(均 $P>0.05$)。见表2。

2.3 肿瘤标志物水平比较

高血糖组术前CEA水平、CA199水平高于血糖正常组,差异均有统计学意义(均 $P<0.05$);2组术前CA125水平、CA242水平、CA724水平、CA50水平比较,差异均无统计学意义(均 $P>0.05$)。2组术后检测结果均较术前下降,但2组术后检测结果比较,差异均无统计学意义(均 $P>0.05$)。见表3。

2.4 术前CA199、CEA水平在各病理分期比较

2组术前CA199在组内不同病理分期比较,差异均有统计学意义(均 $P<0.05$)。高血糖组术前CEA水平在不同病理分期比较,差异有统计学意义($P<0.05$);血糖正常组术前CEA水平不同病理分期比较,差异无统计学意义($P>0.05$)。见表4。

2.5 2组患者术后并发症比较

高血糖组术后并发症发生率高于血糖正常组,差异有统计学意义($P<0.05$)。见表5。

表 1 2组患者临床资料比较

Table 1 Comparison of clinical data between two groups

| Item | Hyperglycemia group(n=36) | Normal blood glucose group(n=42) | χ^2/t | P value |
|--|---------------------------|----------------------------------|------------|---------|
| Gender[n(%)] | | | 0.829 | 0.478 |
| Male | 25(69.4) | 25(59.5) | | |
| Female | 11(30.6) | 17(40.5) | | |
| Age(years, $\bar{x}\pm s$) | 67.94±6.90 | 66.40±4.96 | 1.142 | 0.257 |
| Smoking[n(%)] | 27(75.0) | 30(71.4) | 0.126 | 0.801 |
| Drinking[n(%)] | 20(55.6) | 25(59.5) | 0.125 | 0.819 |
| Basic disease[n(%)] | | | | |
| Hypertension | 22(61.1) | 30(71.4) | 0.929 | 0.470 |
| Hyperlipidemia | 26(72.2) | 28(66.7) | 0.281 | 0.631 |
| Lung diseases | 13(36.1) | 20(47.6) | 1.052 | 0.362 |
| Coronary heart diseases | 8(22.2) | 12(28.6) | 0.410 | 0.608 |
| Cerebrovascular diseases | 21(58.3) | 20(47.6) | 0.892 | 0.372 |
| BMI(kg/m ² , $\bar{x}\pm s$) | 24.61±2.92 | 23.17±2.25 | 2.461 | 0.016 |
| Length of stay(d, $\bar{x}\pm s$) | 15.28±2.25 | 14.69±2.96 | 0.973 | 0.333 |
| Operation time(min, $\bar{x}\pm s$) | 210.92±18.47 | 203.38±19.22 | 1.758 | 0.083 |
| Intraoperative blood loss[n(%)] | | | 0.037 | 0.848 |
| <500 ml | 25(69.4) | 30(71.4) | | |
| ≥500 ml | 11(30.6) | 12(28.6) | | |
| First symptom[n(%)] | | | 17.184 | 0.034 |
| Abdominal pain | 2(5.6) | 9(21.4) | | |
| Abdominal distension | 4(11.1) | 5(11.9) | | |
| Abdominal mass | 4(11.1) | 7(16.7) | | |
| Diarrhea | 6(16.7) | 2(4.8) | | |
| Constipation | 7(19.4) | 2(4.8) | | |
| Bloody stool | 3(8.3) | 5(11.9) | | |
| Weight loss | 2(5.6) | 3(7.1) | | |
| Change in bowel habits | 7(19.4) | 2(4.8) | | |
| Other symptoms | 1(2.8) | 4(9.5) | | |
| No symptom | 0(0.0) | 3(7.1) | | |

BMI: body mass index.

表 2 2组患者病理特征比较

Table 2 Comparison of pathological characteristics between two groups

[n(%)]

| Item | Hyperglycemia group(n=36) | Normal blood glucose group(n=42) | χ^2 | P value |
|---------------------------|---------------------------|----------------------------------|----------|---------|
| Tumor location | | | 3.174 | 0.652 |
| Rectum | 13(36.1) | 17(40.5) | 0.156 | 0.816 |
| Colon | 23(63.9) | 25(59.5) | | |
| Right colon | 6(16.7) | 15(35.7) | 5.598 | 0.023 |
| Left colon | 17(47.2) | 10(23.8) | 1.685 | 0.031 |
| Pathological types | | | 0.528 | 0.593 |
| Adenocarcinoma | 34(94.4) | 41(97.6) | | |
| Mucinouscar cinoma | 2(5.6) | 1(2.4) | | |
| Pathological stage | | | 9.631 | 0.019 |
| I | 1(2.8) | 5(11.9) | | |
| II | 9(25) | 12(28.6) | | |
| III | 14(38.9) | 22(52.4) | | |
| IV | 12(33.3) | 3(7.1) | | |
| Differentiation degree | | | 3.252 | 0.212 |
| Well | 5(13.9) | 2(4.8) | | |
| Middle | 23(63.9) | 34(80.9) | | |
| Low | 8(22.2) | 6(14.3) | | |
| Maximum diameter of tumor | | | 0.601 | 0.497 |
| <5 cm | 22(61.1) | 22(52.4) | | |
| ≥5 cm | 14(38.9) | 20(47.6) | | |
| Tumor shape | | | 0.015 | 1.000 |
| Ulcerative type | 27(75) | 32(76.2) | | |
| Mass type | 9(25) | 10(23.8) | | |
| Margin | | | 0.003 | 1.000 |
| Negative | 31(86.1) | 36(85.7) | | |
| Positive | 5(13.9) | 6(14.3) | | |
| Lymphatic metastasis | | | 4.110 | 0.043 |
| Yes | 22(61.1) | 16(38.1) | | |
| No | 14(38.9) | 26(61.9) | | |

表3 2组患者肿瘤标志物测定结果比较

Table 3 Comparison of tumor markers between two groups

[M(Q₁, Q₃)]

| Item | Before surgical treatment | | | | After surgical treatment | | | |
|-------------|----------------------------|-----------------------------------|-------|---------|----------------------------|-----------------------------------|-------|---------|
| | Hyperglycemia group (n=36) | Normal blood glucose group (n=42) | Z | P value | Hyperglycemia group (n=36) | Normal blood glucose group (n=42) | Z | P value |
| CEA(ng/ml) | 18.30(454.30,3.87) | 7.25(274.50,1.66) | -2.40 | 0.017 | 3.00(135.20,0.80) | 2.75(106.00,0.50) | -1.01 | 0.314 |
| CA125(U/ml) | 30.37(76.78,7.39) | 25.24(78.69,6.13) | -0.98 | 0.326 | 12.38(57.73,5.05) | 10.80(52.93,3.02) | -1.03 | 0.302 |
| CA199(U/ml) | 103.73(981.00,13.26) | 75.34(225.80,11.12) | -2.14 | 0.033 | 37.57(591.10,4.40) | 35.51(97.80,6.40) | -1.38 | 0.167 |
| CA242(U/ml) | 10.64(141.42,0.85) | 6.52(166.80,0.80) | -1.11 | 0.269 | 4.32(54.87,1.56) | 5.08(22.64,1.62) | -0.91 | 0.366 |
| CA724(U/ml) | 20.83(93.30,1.51) | 15.71(140.90,1.01) | -1.81 | 0.071 | 8.76(50.10,1.03) | 5.09(44.75,0.61) | -1.10 | 0.272 |
| CA50(U/ml) | 13.70(500,2.02) | 11.96(38.57,0.50) | -1.20 | 0.229 | 5.68(27.69,1.91) | 8.32(61.34,0.55) | -1.04 | 0.297 |

表4 2组患者术前CA199、CEA水平在各病理分期比较

Table 4 Comparison of CA199 and CEA levels before operation between two groups

[M(Q₁, Q₃)]

| Pathological stage | CA199(μ/ml) | | CEA(ng/ml) | |
|--------------------|----------------------------|-----------------------------------|----------------------------|-----------------------------------|
| | Hyperglycemia group (n=36) | Normal blood glucose group (n=42) | Hyperglycemia group (n=36) | Normal blood glucose group (n=42) |
| I | 27.62(27.62,27.62) | 23.28(32.32,11.12) | 13.80(13.80,13.80) | 5.30(68.62,2.28) |
| II | 56.57(154.74,13.26) | 38.25(99.50,15.45) | 15.95(113.82,5.72) | 10.62(83.11,1.66) |
| III | 72.42(200.30,27.68) | 80.04(225.80,13.15) | 18.30(93.20,3.87) | 11.87(93.37,1.79) |
| IV | 138.28(1000.00,62.95) | 131.10(200.70,87.31) | 86.33(454.30,38.62) | 35.30(129.60,8.21) |
| Z | 10.54 | 19.73 | -16.74 | -7.861 |
| P value | 0.015 | 0.020 | 0.011 | 0.350 |

表5 2组患者术后并发症比较

Table 5 Comparison of postoperative complications between two groups

[n(%)]

| Group | n | Pulmonary infection | Surgical incision infection | Anastomotic leakage | Wound dehiscence | Intestinal obstruction | Urinary retention | Deep venous thrombosis | Complication rate |
|----------------------|----|---------------------|-----------------------------|---------------------|------------------|------------------------|-------------------|------------------------|-------------------|
| Hyperglycemia | 36 | 5(13.9) | 3(8.3) | 2(5.6) | 2(5.6) | 0(0.0) | 0(0.0) | 0(0.0) | 12(33.4) |
| Normal blood glucose | 42 | 2(4.8) | 1(2.4) | 1(2.4) | 0(0.0) | 4(9.5) | 2(4.8) | 2(4.8) | 12(28.7)* |

Compared with hyperglycemia group, $\chi^2=3.241$, * $P=0.035<0.05$.

3 讨论

由于结直肠癌早期临床表现不典型,很多老年人易忽略症状,等到瘤体较大,腹痛症状较重,腹部可扪及包块时,才主动就诊。本研究显示,血糖正常组首发症状以腹痛、腹部包块及腹胀多见;高血糖组首发症状以便秘、排便习惯改变、腹泻多见,可能与自主神经和肠神经病变有关,导致结肠动力下降,肠道内物质蓄积,引起便秘^[5]。高血糖者更易腹泻的原因有多种,其中由降糖药物二甲双胍导致的吸收性腹泻最常见^[6]。另外,高血糖刺激肠道细菌过度生长、胆汁酸吸收障碍和艰难梭菌感染引起结肠炎等也会造成腹泻^[5]。

本研究以脾区为分界,将结肠划分为左半结肠与右半结肠。本研究结果显示,高血糖组结直肠癌多位于左半结肠,血糖正常组结直肠癌多位于右半结肠。推测可能与体内高血糖环境下,乙状结肠易于蓄积致癌物质,结肠远端上皮细胞对致癌物质敏

感性增强有关^[7]。国外有研究指出,与血糖正常者相比,高血糖者的淋巴结转移比例更高^[8],本研究结果与之一致,且高血糖组 BMI 更高。2 组肿瘤病理分期结果显示:高血糖组病理分期多位于 III、IV 期,血糖正常组多位于 II、III 期,可能是由于高血糖诱导通过 TGF-β/PI3/AKT 途径和上调血红素加氧酶表达,增强肿瘤细胞迁移能力^[9],促进了淋巴结转移。炎症刺激会诱导肿瘤的发生和进展,而高血糖状态促进炎症因子的分泌^[10],亦有研究表明,高血糖通过代谢和分子改变或基因突变促进恶性肿瘤细胞增殖^[11],而且高血糖能够提供肿瘤细胞快速增殖所需的更多能量,癌细胞增殖更快^[12],增强了肿瘤细胞的侵袭能力。

高血糖状态下,部分胰腺组织细胞被脂肪空泡细胞所取代,胰岛内淀粉样物质发生玻璃样变,促进 CA199 释放入血,在本研究中,高血糖组术前 CA199 水平更高,验证了这一理论。CEA 对结直肠、胃等内

胚叶上皮演化而来的肿瘤较为敏感,2组术前CEA水平对比,老年结直肠癌高血糖组术前CEA水平明显升高,这可能是由于体内高血糖环境增加氨基己糖生物合成途径的活性,促进细胞增殖、侵袭和迁移,诱导CEA表达^[13],行手术治疗后CEA水平降低^[14],与本研究结果一致。进一步对比2组各病理分期术前CA199和CEA水平,发现无论血糖水平是否正常,老年结直肠癌患者术前CA199水平均随病理分期进展而升高,表明术前CA199水平在一定程度上反映老年结直肠癌的病理分期。本研究的高血糖组术前CEA水平与肿瘤分期相关,肿瘤分期越晚,CEA水平越高,因此,CEA水平可作为判断老年高血糖组肿瘤病理分期的重要评估指标。而血糖正常组术前CEA水平在各病理分期无明显差异,这与Topdagi等^[15]学者的研究一致,认为CEA水平与患者的病理分期之间没有明确的相关性。

本研究结果表明,高血糖组术后感染发生率高于血糖正常组,可能是由于高血糖者免疫功能受损,引起中性粒细胞免疫衰老,造成趋化性障碍,吞噬能力降低和杀菌活性降低等^[16]。此外,高血糖提供了一个富含营养物质的内环境,增加了微生物致病菌株的定殖率,导致感染的发生。早在20世纪,Black等^[17]指出,高血糖状态会加速蛋白质的非酶糖基化,从而使免疫球蛋白失活,并阻碍细菌的自我调理作用,从而诱发感染。

综上,高血糖状态是老年结直肠癌的危险因素,与其临床症状、病理特征密切相关。术后并发症更倾向于肺部感染和手术切口感染,在合并血糖升高的老年结直肠癌患者中进行控制血糖的宣教,可降低术后感染率。

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