

术后早期血糖异常对食管癌根治术患者短期预后的预测价值

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【摘要】 目的 分析食管癌根治术后早期血糖异常对术后短期预后的评估价值。**方法** 回顾性研究复旦大学附属中山医院2015年4月至2017年9月的308例食管癌根治术患者的住院病例,收集人口学特征、术前三项已知的基础病、术前空腹血糖、术后早期血糖值及术后住院期间的短期临床不良事件等数据。308例中1例术后早期发生低血糖(3.8 mmol/L),未单独成组。307例患者按术后早期血糖分为正常血糖组($n=215$)和高血糖组($n=92$)。另以前术前的空腹血糖为基础血糖,分为术后血糖升高较多组(≥ 4 mmol/L, $n=52$)及血糖升高较少组(< 4 mmol/L, $n=255$)。**结果** 采用分层 χ^2 检验进行术后早期高血糖与各术后临床不良事件的风险评估,差异无统计学意义。多元Logistics回归处理混杂因素后发现,血糖波动大是术后不良事件总发生率的危险因素($P=0.003$, OR=2.641, 95%CI: 1.402~4.976),血糖波动大亦是病死率的危险因素($P=0.012$, OR=7.539, 95%CI: 1.534~36.713)。**结论** 术后早期血糖较术前空腹血糖波动较大可以预测食管癌根治术后短期预后不良。

【关键词】 食管癌根治术; 术后; 血糖; 短期预后

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The value of abnormal early postoperative blood glucose concentration in predicting the short-term outcome of patients after radical resection of esophageal cancer

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【Abstract】 Objective To analyze the relationship between the short-term outcomes and abnormal early postoperative blood glucose concentration of patients after radical resection of esophageal cancer. **Methods** We conducted a retrospective cohort analysis of 308 patients who underwent radical resection of esophageal cancer between Apr. 2015 and Sep. 2017 in Zhongshan Hospital, Fudan University. These materials were including demographic characteristics, known preoperatively previous medical history (PMH), fasting blood glucose before operation, early postoperative blood glucose concentration and short-term clinical adverse events during hospitalization. Among the 308 cases, 1 patient developed hypoglycemia (3.8 mmol/L), which was not isolated into a group. The other 307 patients were divided into two groups according to the early postoperative blood glucose values: normal blood glucose group ($n=215$) and

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hyperglycemia group ($n=92$). In addition, based on the fasting blood glucose before operation, the patients were divided into the group with higher postoperative blood glucose fluctuation (≥ 4 mmol/L, $n=52$) and the group with lower blood glucose fluctuation (< 4 mmol/L, $n=255$). **Results** No statistical difference was found between early postoperative hyperglycemia and postoperative adverse events by stratified Person Chi-Square test. Using multivariate Logistics regression to deal with confounding factors, the blood glucose fluctuation was a risk factor. The incidence of postoperative adverse events was higher in the higher glucose fluctuation group than that in the lower glucose fluctuation group using preoperative fasting blood glucose concentration as baseline ($P=0.003$, $OR=2.641$, 95%CI: 1.402–4.976). Mortality was higher in the higher glucose fluctuation group than in the lower glucose fluctuation group using preoperative fasting blood glucose as baseline ($P=0.012$, $OR=7.539$, 95%CI: 1.534–36.713). **Conclusion** Early high postoperative blood glucose fluctuation may be a predictor for poor short-term outcomes of patients after radical resection of esophageal cancer.

【Key words】 radical resection of esophageal cancer; postoperation; blood glucose; short-term outcome

随着腔镜手术的开展和麻醉技术的不断更新,食管癌手术患者术后临床不良事件发生率明显下降^[1-2]。围术期血糖管理仍是关系预后的重要环节,血糖异常(高血糖、血糖波动和低血糖)则是影响手术患者短期预后不良的因素^[3-9],有研究认为加强血糖控制有利于改善患者预后^[10-11]。既往血糖与预后的研究多针对心血管疾病或急诊重症患者^[11,16],目前关于食管癌患者围术期血糖管理的研究甚少。本研究旨在探讨术后早期血糖异常对食管癌根治术患者术后短期预后的预测价值,为进一步研究食管癌根治术患者术后血糖管理方案提供临床医学证据。

资料和方法

资料收集及分组 回顾性收集复旦大学附属中山医院2015年4月至2017年9月行食管癌根治术患者的住院病例,排除有严重系统疾病者、年龄 > 80 岁及病史资料缺失的患者。收集的数据包括人口学特征和术前已知的夹杂症(呼吸系统疾病、心脏病、高血压、糖尿病等),采集病史中术后入外科监护室后第1个血糖值,术后伤口恢复情况(包括有无感染),肺部感染情况(具备影像学证据并有临床表现等),食管瘘,乳糜胸,心血管意外发生情况(术后发生心律失常、心跳骤停、心衰等),其他并发症(脏器功能衰竭、术后出血、喉返神经损伤等),外科监护室住院天数,总住院天数,病死率,术后抗生素

使用情况等。

高血糖评价标准根据2015年版围术期血糖管理专家共识^[12],推荐监护室患者血糖控制低于8.4 mmol/L。按照入外科监护室后第1个血糖值分为正常血糖(NG)组及高血糖(HG)组。

以术前空腹血糖为基础血糖,将患者按照手术前后血糖值差分组。根据2015年版围术期血糖管理专家共识^[12],术后血糖高于10.0 mmol/L需胰岛素治疗以稳定血糖,考虑术前血糖正常值上限为6.1 mmol/L,据此取差值4 mmol/L。将患者分为术后血糖升高较小组(< 4 mmol/L, A组)和术后血糖升高较大组(≥ 4 mmol/L, B组)。

统计学分析 本研究采用SPSS 20.0统计软件进行统计分析。连续变量表示为 $\bar{x} \pm s$,用 t 检验进行评价;分类变量表示为频率和百分比,用 χ^2 检验和Wilcoxon秩和检验分析;用多元Logistic回归校正混杂因素。 $P < 0.05$ 为差异有统计学意义。

结 果

术后高血糖组与正常血糖组患者的基本资料 共308例患者入组,其中1例术后血糖值为3.8 mmol/L,未单独成组。其余307例患者分为正常血糖组(NG组, $n=215$)及高血糖组(HG组, $n=92$),正常血糖组包括正常低值血糖(≤ 5.6 mmol/L, $n=24$),高血糖组包括严重高血糖(≥ 11.1 mmol/L, $n=5$)(表1)。两组间年龄($P < 0.001$)、性别($P=0.001$)及

是否合并糖尿病($P=0.004$)差异有统计学意义。高血糖组患者年龄较大,女性比例较高,合并糖尿病患者比例较高。

表 1 正常血糖组与高血糖组患者的基本资料

Tab 1 Characteristics of patients in hyperglycemia group and normal blood glucose groups [n (%) or $\bar{x} \pm s$]

Item	HG ($n=92$)	NG ($n=215$)	P
Age (y)	64.3 \pm 6.8	60.9 \pm 7.3	<0.001
Male	63 (68.5)	183 (85.1)	0.001
BMI (kg/m ²)	22.7 \pm 3.2	23.3 \pm 8.8	0.562
Other preoperative treatments ⁽¹⁾	12 (13.0)	26 (12.1)	0.817
PMH			
Diabetes mellitus	13 (14.1)	10 (4.7)	0.004
Hypertension	26 (28.3)	56 (26.0)	0.688
Cardiovascular disease	4 (4.3)	11 (5.1)	0.775
Chronic bronchitis	1 (1.1)	1 (0.5)	0.536
Stroke	5 (5.4)	4 (1.9)	0.090

⁽¹⁾Including chemoradiotherapy and ESD surgery.HG:Hyperglycemia group;NG:Normal blood glucose group;BMI:Body mass index;ESD:Endoscopic submucosal dissection;PMH: Previous medical history. Wilcoxon rank sum test was used for classified variables, and t test was used for continuous variables.

术后血糖值与各项结局及死亡率 分析高血

表 2 高血糖与短期预后的相关性

Tab 2 Correlation between hyperglycemia and short-term outcomes [n (%) or $\bar{x} \pm s$]

Item	HG ($n=92$)	NG ($n=215$)	P	OR	95%CI
Wound infection	7 (7.6)	20 (9.3)	0.631	0.803	0.327-1.970
Pulmonary infection	14 (15.2)	39 (18.1)	0.535	0.810	0.416-1.577
Anastomotic fistula	9 (9.8)	28 (13.0)	0.424	0.724	0.327-1.602
Chylothorax	0 (0)	3 (1.4)	0.557	1.014	0.998-1.030
MACE	6 (6.5)	10 (4.7)	0.499	1.430	0.504-4.058
RF	6 (6.5)	11 (5.1)	0.622	1.294	0.464-3.610
Total incidence of adverse events	38 (41.3)	77 (35.8)	0.363	1.261	0.765-2.079
Mortality	4 (4.3)	3 (1.4)	0.112	3.212	0.704-14.649
Days in SICU (d)	4.73 \pm 4.67	4.17 \pm 4.94	0.355	—	—
Length of stay (d)	22.9 \pm 15.0	23.3 \pm 18.0	0.83	—	—

MACE:Major adverse cardiovascular events;RF:Respiratory failure.Fisher's exact test was used for frequency<5, χ^2 test was used for risk assessment,and Wilcoxon rank sum test was used for classified variables.

按年龄分层做风险评估 对于60岁以下患者中呼吸功能衰竭致术后使用呼吸机这个结局,血糖波动是一个显著相关危险因素($P=0.044$,OR=11.625,95%CI:1.440~93.871);对于60~70岁患者中不良事件总发生率这个结局,血糖波动是一个中等相关危险因素($P=0.029$,OR=2.296,95%CI:1.078~4.890)(表10)。

糖与各项结局包括伤口感染、呼吸系统感染、吻合口瘘、乳糜胸、心血管不良事件、ARDS、死亡率的关系,未发现术后早期高血糖为食管癌根治术后预后不良的危险因素(表2)。

按年龄、性别、是否合并糖尿病病史分层进行风险评估,也未发现术后早期高血糖为食管癌根治术后预后不良的危险因素(表3~5)。

按血糖波动分组患者的基本资料 307例患者以术前、术后血糖值差分组,血糖升高<4 mmol/L(A)组255例,血糖升高 ≥ 4 mmol/L(B)组52例。两组间年龄($P=0.020$)和性别($P=0.017$)差异均有统计学意义。B组患者年龄较大,女性占比更高(表6)。

血糖波动与各项结局 采用 χ^2 检验分析食管癌根治术后短期预后的各项结局与血糖波动值的关系,发现不良事件总发生率($P=0.001$,OR=2.727,95%CI:1.484~5.013)和病死率($P=0.004$,OR=7,95%CI:1.518~32.277)差异均有统计学意义(表7)。针对不良事件总发生率和病死率这两个结局,将各种危险因素放入多元Logistics回归模型中,发现血糖波动大这个危险因素的OR值分别为2.641($P=0.003$,95%CI:1.402~4.976)和7.539($P=0.012$,95%CI:1.534~36.713)(表8~9)。

讨 论

食管癌是我国恶性肿瘤中死亡顺位排名第4的恶性肿瘤,是预后较差的消化系统肿瘤^[13],通过外科技技术、麻醉管理的提高及术后监护室的支持,有助于改善食管癌患者短期预后。其中一项重要组

表3 按性别分层后高血糖与短期预后的相关性

Tab 3 Correlation between hyperglycemia and poor short-term outcomes after stratification by gender [n (%)]

Item	HG (n=92)	NG (n=215)	P	OR	95%CI
Wound infection					
Male	5 (7.9)	14 (7.3)	0.941	1.041	0.359-3.015
Female	2 (6.9)	6 (18.8)	0.171	0.321	0.059-1.737
Pulmonary infection					
Male	10 (15.9)	32 (17.5)	0.769	0.890	0.410-1.934
Female	4 (13.8)	7 (21.9)	0.412	0.571	0.148-2.199
Anastomotic fistula					
Male	7 (11.1)	25 (13.7)	0.604	0.790	0.324-1.927
Female	2 (6.9)	3 (9.4)	0.725	0.716	0.111-4.620
Chylothorax					
Male	0 (0)	3 (1.6)	0.572	1.017	0.998-1.036
Female	0 (0)	0 (0)	-	-	-
MACE					
Male	4 (6.3)	8 (4.4)	0.530	1.483	0.431-5.104
Female	2 (6.9)	2 (6.3)	0.919	1.111	0.146-8.441
RF					
Male	6 (9.5)	10 (5.5)	0.251	1.821	0.634-5.232
Female	0 (0)	1 (3.1)	1.000	1.032	0.970-1.099
Total incidence of adverse events					
Male	27 (42.8)	64 (34.9)	0.264	1.395	0.778-2.010
Female	11 (37.9)	13 (40.6)	0.830	0.893	0.319-2.501
Mortality					
Male	3 (4.8)	3 (1.6)	0.166	3.000	0.590-15.262
Female	1 (3.4)	0 (0)	0.475	0.966	0.901-1.034

χ^2 test was used for risk assessment, and Fisher's exact test was used for frequency < 5. MACE: Major adverse cardiovascular events; RF: Respiratory failure. Male in HG group: n=63; Female in HG group: n=29; Male in NG group: n=183; Female in NG group: n=32.

表4 按合并糖尿病与否分层后高血糖与短期预后的相关性

Tab 4 Correlation between hyperglycemia and short-term outcomes after stratification by diabetes mellitus [n (%)]

Item	HG (n=92)	NG (n=215)	P	OR	95%CI
Wound infection					
Diabetes	1 (7.7)	1 (10.0)	0.846	0.750	0.041-13.677
Non-diabetes	6 (7.6)	19 (9.3)	0.656	0.321	0.309-2.095
Pulmonary infection					
Diabetes	1 (7.7)	4 (40.0)	0.063	0.125	0.011-1.379
Non-diabetes	13 (16.5)	35 (17.1)	0.901	0.957	0.476-1.921
Anastomotic fistula					
Diabetes	1 (7.7)	1 (10.0)	0.846	0.750	0.041-13.677
Non-diabetes	8 (10.1)	27 (13.2)	0.484	0.743	0.322-1.713
Chylothorax					
Diabetes	0 (0)	0 (0)	-	-	-
Non-diabetes	0 (0)	3 (1.5)	0.280	1.015	0.998-1.032
MACE					
Diabetes	1 (7.7)	0 (0)	0.370	0.923	0.789-1.080
Non-diabetes	5 (6.3)	10 (4.9)	0.624	1.318	0.436-3.983
RF					
Diabetes	0 (0)	1 (10.0)	0.435	1.111	0.904-1.366
Non-diabetes	6 (7.6)	10 (4.9)	0.374	1.603	0.562-4.567
Total incidence of adverse events					
Diabetes	4 (30.7)	5 (50.0)	0.349	0.444	0.080-2.457
Non-diabetes	34 (43.0)	72 (35.1)	0.216	1.396	0.822-2.370
Mortality					
Diabetes	0 (0)	0 (0)	-	-	-
Non-diabetes	4 (5.1)	3 (1.5)	0.080	3.591	0.785-16.423

Diabetes in HG group: n=13; Non-diabetes in HG group: n=79; Diabetes in NG group: n=10; Non-diabetes in NG group: n=205. Others were as same as Tab 3.

表5 按年龄分层后高血糖与短期预后的相关性

Tab 5 Correlation between hyperglycemia and short-term outcomes after stratification by age [n (%) or $\bar{x} \pm s$]

Item	HG (n=92)	NG (n=215)	P	OR	95%CI
Wound infection					
<60 y	2 (9.1)	5 (6.0)	0.635	1.560	0.282-8.641
60-70 y	5 (9.1)	12 (10.7)	0.744	0.833	0.278-2.496
>70 y	0	3 (15.0)	0.244	1.176	0.979-1.414
Pulmonary infection					
<60 y	4 (18.2)	14 (16.9)	1.000	1.095	0.321-3.733
60-70 y	6 (10.9)	20 (17.9)	0.244	0.563	0.212-1.495
>70 y	4 (26.7)	5 (25.0)	1	1.091	0.237-5.027
Anastomotic fistula					
<60 y	1 (4.5)	11 (13.3)	0.453	0.312	0.038-2.556
60-70 y	6 (10.9)	13 (11.6)	0.894	0.932	0.334-2.602
>70 y	2 (13.3)	4 (20.0)	0.680	0.615	0.097-3.908
Chylothrax					
<60 y	0 (0)	2 (2.4)	1.000	1.025	0.991-1.060
60-70 y	0 (0)	0 (0)	1.000		
>70 y	0 (0)	1 (5.0)	0.557	1.053	0.952-1.164
MACE					
<60 y	0 (0)	3 (3.6)	1.000	1.038	0.995-1.082
60-70 y	3 (5.5)	3 (2.7)	0.397	2.096	0.409-9.763
>70 y	3 (20.0)	4 (20.0)	1.000	1.000	0.188-5.332
RF					
<60 y	2 (9.1)	2 (2.4)	0.193	4.050	0.537-30.534
60-70 y	3 (5.5)	6 (5.4)	1	1.019	0.245-4.238
>70 y	1 (6.7)	3 (15.0)	0.619	0.405	0.038-4.335
Total incidence of adverse events					
<60 y	9 (40.9)	27 (32.5)	0.462	1.436	0.546-3.773
60-70 y	22 (40.0)	42 (37.5)	0.755	1.111	0.574-2.153
>70 y	7 (46.7)	8 (40.0)	0.693	1.313	0.339-5.076
Mortality					
<60 y	1 (4.5)	2 (2.4)	0.510	1.929	0.167-22.304
60-70 y	2 (3.6)	0 (0)	0.107	0.964	0.915-1.014
>70 y	1 (6.7)	1 (5.0)	1.000	1.357	0.078-23.615

<60 y in HG group: n=22; 60-70 y in HG group: n=55; >70 y in HG group: n=15; <60 y in NG group: n=83; 60-70 y in NG group: n=112; >70 y in NG group: n=20. Others were as the same as Tab 3.

表6 血糖波动较大组与血糖波动较小组患者的基本资料

Tab 6 Characteristics of patients in higher and lower blood glucose fluctuation groups [n (%) or $\bar{x} \pm s$]

Item	Group A (n=255)	Group B (n=52)	P
Age (y)	61.5 \pm 7.5	64.1 \pm 6.18	0.020
Male	208 (81.6)	38 (73.1)	0.017
BMI (kg/m ²)	23.2 \pm 8.2	22.5 \pm 2.8	0.505
Other preoperative treatments ⁽¹⁾	30 (11.8)	12 (23.1)	0.471
PMH			
Diabetes	16 (6.3)	7 (13.5)	0.073
Hypertension	67 (26.2)	15 (28.8)	0.703
Cardiovascular disease	14 (5.5)	1 (1.9)	0.278
Chronic bronchitis	1 (0.4)	1 (1.9)	0.212
Stroke	7 (2.7)	2 (3.8)	0.668

⁽¹⁾Including chemoradiotherapy and ESD surgery. Group A: Higher blood glucose fluctuation group (≥ 4 mmol/L); Group B: Lower blood glucose fluctuation group (< 4 mmol/L). Wilcoxon rank sum test was used for classified variables, and *t* test was used for continuous variables.

成部分就是围术期的血糖管理。虽有文献阐述围术期血糖值的异常(高血糖、低血糖和血糖波动)与患者预后不良的相关性^[4,9,11,14],但尚缺乏食管癌方面的资料。

本研究同时纳入糖尿病患者和非糖尿病患者,其中7例住院期间死亡的患者均为非糖尿病患者。有研究在其他手术围术期也发现非糖尿病患者的风险高于糖尿病患者,并解释可能是由于实际临床工作中术前已知的糖尿病患者更容易得到关注及治疗^[4]。故而,非糖尿病患者的围术期血糖管理同样值得我们重视。

关于早期高血糖与患者预后相关性的研究结果并不一致。Kutz等^[11]的研究纳入了7 132名急诊科患者,认为早期高血糖与患者预后不良相关。van den Berghe等^[15]的应用胰岛素控制血糖,认为严

表7 血糖波动与短期预后的相关性

Tab 7 Correlation between blood glucose fluctuation and short-term outcomes

[n (%) or $\bar{x} \pm s$]

Item	Group B (n=52)	Group A (n=255)	P	OR	95%CI
Wound infection	5 (10.0)	22 (8.6)	0.819	1.127	0.406-3.126
Pulmonary infection	13 (25.0)	40 (15.7)	0.105	1.792	0.879-3.654
Anastomotic fistula	9 (17.3)	28 (11.0)	0.202	1.697	0.748-3.848
Chylothra	0 (0)	3 (1.2)	1.000	1.012	0.998-1.026
MACE	4 (7.7)	12 (4.7)	0.377	1.688	0.522-5.454
RF	5 (9.6)	12 (4.7)	0.158	2.154	0.725-6.401
Total incidence of adverse events	30 (57.6)	85 (33.3)	0.001	2.727	1.484-5.013
Mortality	4 (7.7)	3 (1.2)	0.004	7.000	1.518-32.277
Days in SICU(d)	5.58 \pm 5.862	4.08 \pm 4.597	0.088	-	-
Length of stay(d)	26.44 \pm 18.547	22.53 \pm 16.786	0.163	-	-

Fisher's exact test was used for frequency < 5 , and χ^2 test was used for risk assessment. Wilcoxon rank sum test was used for classified variables, and t test was used for continuous variables. Group A: Higher blood glucose fluctuation group (≥ 4 mmol/L); Group B: Lower blood glucose fluctuation group (< 4 mmol/L). MACE: Major adverse cardiovascular events; RF: Respiratory failure.

表8 按年龄分层后血糖波动与短期预后的相关性

Tab 8 Correlation between blood glucose fluctuation and short-term outcomes after stratification by age

[n (%)]

Item	Group B (n=52)	Group A (n=255)	P	OR	95%CI
Wound infection					
<60 y	0 (0)	7 (7.4)	1.000	1.080	1.020-1.143
60-70 y	5 (14.3)	12 (9.1)	0.366	1.667	0.545-5.095
>70 y	0 (0)	3 (10.7)	1.000	1.120	0.985-1.273
Pulmonary infection					
<60 y	4 (40)	14 (14.7)	0.066	3.857	0.964-15.432
60-70 y	6 (17.1)	20 (15.2)	0.773	1.159	0.426-3.148
>70 y	3 (42.9)	6 (21.4)	0.340	2.750	0.479-15.794
Anastomotic fistula					
<60 y	1 (10.0)	11 (11.5)	1.000	0.848	0.098-7.353
60-70 y	6 (17.1)	13 (9.8)	0.227	1.894	0.663-5.407
>70 y	2 (28.6)	4 (14.3)	0.576	2.400	0.341-16.899
Chylothra					
<60 y	0 (0)	2 (2.1)	1.000	1.022	0.992-1.052
60-70 y	0 (0)	0 (0)	1.000	1.037	0.966-1.114
>70 y	0 (0)	1 (3.6)	1.000	1.012	0.998-1.026
MACE					
<60 y	0 (0)	3 (3.2)	1.000	1.033	0.996-1.071
60-70 y	3 (8.6)	3 (2.3)	0.107	4.031	0.777-20.916
>70 y	1 (14.3)	6 (21.4)	1.000	0.611	0.061-6.104
RF					
<60 y	2 (20.0)	2 (2.1)	0.044	11.625	1.440-93.871
60-70 y	2 (5.7)	7 (5.3)	1.000	1.082	0.215-5.456
>70 y	1 (14.3)	3 (10.7)	1.000	1.389	0.122-15.812
Total incidence of adverse events					
<60 y	6 (60.0)	30 (31.6)	0.088	3.250	0.853-12.376
60-70 y	19 (54.3)	45 (34.1)	0.029	2.296	1.078-4.890
>70 y	5 (71.4)	10 (35.7)	0.112	4.500	0.734-27.577
Mortality					
<60 y	1 (10.0)	2 (2.1)	0.262	5.167	0.426-62.695
60-70 y	2 (5.7)	0 (0)	0.043	0.943	0.869-1.023
>70 y	1 (14.2)	1 (3.6)	0.365	4.500	0.245-82.568

Group A: Higher blood glucose fluctuation group (≥ 4 mmol/L); Group B: Lower blood glucose fluctuation group (< 4 mmol/L). <60 y in group B: n=10; 60-70 y in group B: n=35; >70 y in group B: n=7; <60 y in group A: n=95; 60-70 y in group A: n=132; >70 y in group A: n=28. Others were as the same as Tab 3.

表9 多元 Logistic 回归校正混杂因素后的术后不良反应事件总发生率

Tab 9 Total incidence of adverse events with multivariate Logistic regression correcting for confounding factors (n=308)

Factors	β (parameter estimate)	P	OR	95%CI
Age	-0.006	0.746	0.994	0.961-1.029
BMI	0.002	0.923	1.002	0.968-1.037
Sex	0.041	0.895	1.042	0.567-1.917
Other preoperative treatments	-0.254	0.486	0.776	0.380-1.585
PMH				
Hypertension	-0.475	0.089	0.622	0.359-1.075
Cardiovascular disease	-0.129	0.823	0.879	0.283-2.727
Stroke	0.021	0.978	1.021	0.244-4.275
Diabetes	0.2	0.679	1.221	0.475-3.139
Glucose fluctuations	0.971	0.003	2.641	1.402-4.976

(¹)Including chemoradiotherapy and ESD surgery. BMI: Body mass index; PMH: Previous medical history.

表10 多元 Logistic 回归校正混杂因素后的病死率

Tab 10 Mortality with multivariate Logistic regression correcting for confounding factors (n=308)

Factors	β (parameter estimate)	P	OR	95%CI
Age	-0.080	0.222	0.923	0.812-1.050
BMI	0.117	0.427	1.127	0.842-1.500
Sex	-0.565	0.616	0.568	0.062-5.176
Other preoperative treatments ^a	0.435	0.714	1.546	0.150-15.891
Hypertension	-1.028	0.233	0.358	0.066-1.936
Glucose fluctuations	2.020	0.012	7.539	1.548-36.713

^aIncluding chemoradiotherapy and ESD surgery. BMI: Body mass index.

格控制危重患者的血糖能够降低发病率和死亡率,从反面论证了高血糖与预后的关系。而 Smith 等^[16]关于高血糖与脑外伤预后的研究结果则显示,外伤后持续 48 h 以上的高血糖与预后差有关系,但早期高血糖与预后的相关性不强。本研究将患者按术后早期血糖分为正常血糖组与高血糖组,按照性别、年龄、糖尿病病史等因素分层进行风险评估,差异无统计学意义,与 Smith 等^[16]的结果较一致。此结果提示,除注意单次高血糖外,更应重视患者是否存在持续性高血糖。

血糖波动的研究起始于一些热衷于用胰岛素控制高血糖以期达到改善预后的研究,在研究过程中意外发现血糖较大波动会增加死亡率和发病率^[17]。有关血糖波动的临床研究中,患者多为急性或危重患者,重症患者的血糖控制目标已有报道,而择期手术患者中血糖波动的研究尚不多见,目前尚无理想的血糖控制目标,故采用适当宽松的血糖

控制方案^[12]。本研究发现以术前空腹血糖值为基础,术后早期血糖升高幅度较大(≥ 4 mmol/L)是术后短期不良事件总发生率、病死率的危险因素。在校正性别、年龄等混杂因素后,针对术后不良事件总发生率这个结局,术后血糖升高幅度较大是中等相关的危险因素,而针对病死率这个结局,则是强相关的危险因素。另外,我们发现术后早期血糖升高幅度较大是 60 岁以下患者术后发生呼吸功能衰竭而使用呼吸机的强相关危险因素。

根据 Quagliaro 等^[6-7]的研究结论:在体外环境中稳定的高血糖与间歇性高血糖(即血糖波动)同样造成内皮细胞损伤,而间歇性高血糖环境中内皮功能障碍、氧化应激反应及凋亡表现更为明显。本研究选择食管癌根治术患者作为研究对象,手术创伤大、患者焦虑紧张、麻醉和术后疼痛等均可引起糖代谢异常^[3],促使血管内皮功能障碍,加速脂肪分解,产生过量的游离脂肪酸^[4],引起白细胞吞噬能力和伤口愈合速度明显下降等^[5],其与术后短期并发症及死亡有关。根据以上研究,我们认为术后早期血糖较术前基础血糖升高幅度较大的情况下,食管癌根治术后不良事件发生率更高,对于预测术后短期预后不良有一定价值,为下一步研究食管癌根治术患者围术期血糖控制目标,以减少术后患者血管内皮损伤等障碍及降低并发症发生率提供了临床依据。

本研究为回顾性队列研究,不足之处在于未能将术后胰岛素使用情况纳入。进一步研究需将实验设计为前瞻性研究,还需控制纳入病例的肿瘤位置、分期、分型及术者等影响预后的混杂因素,且可

在术前检测糖化血红蛋白水平,发现隐匿性糖尿病患者,则结果将更为可靠。

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