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·专题研究·

早发性胰腺癌的临床病理特征及预后的单中心回顾性研究

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摘要

背景与目的：胰腺癌是一种恶性程度极高、预后极差的消化系统肿瘤。近年来其发病呈年轻化趋势，早发性胰腺癌（EOPC，诊断年龄≤50岁）比例逐年上升，可能具有独特的生物学行为和预后特征。国内针对EOPC的系统研究较少，因此本研究探讨EOPC患者的临床病理特征及其预后。

方法：回顾性分析2017年1月—2023年12月中南大学湘雅医院收治的113例EOPC患者的临床资料，包括一般资料、临床病理特征及预后信息。采用Kaplan-Meier法绘制生存曲线，并比较手术组与非手术组的生存差异。

结果：113例EOPC患者中位年龄为46（42~49）岁，男性占65.49%。A型及O型血型占比最高（40.71%和34.51%）。主要临床症状为腹痛（69.91%）、体质量下降（62.83%）、黄疸（43.36%）和腹胀（36.28%）。影像学显示胆管扩张32.74%，主胰管扩张39.82%，血管侵犯59.29%，远处转移52.21%。病理结果显示腺癌及导管腺癌占93.81%，以中、低分化为主（共76.10%），胰头部发病最常见（65.42%）。TNM分期显示，淋巴结转移率高达77.88%，临床IV期占52.21%。实验室检查中CA19-9显著升高。Kaplan-Meier分析显示，全队列中位总生存期为18.6个月；手术组明显优于非手术组（29.4个月 vs. 13.8个月，P=0.0015）。

结论：EOPC患者多为男性，病变好发于胰头部，临床表现隐匿，确诊时多已进展期或伴远处转移，具有分化差、侵袭性强的特点。手术切除显著改善患者生存，是延长预后的关键。年轻人群出现不明原因腹痛、体质量下降或黄疸等症状时，应提高警惕，加强影像学筛查，争取早期诊断与手术机会。未来需开展多中心、大样本前瞻性研究以进一步验证本研究结果。

关键词

胰腺肿瘤；疾病特征；预后

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Clinicopathologic characteristics and prognosis of early-onset pancreatic cancer: a single-center retrospective analysis

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Abstract

Background and Aims: Pancreatic cancer is one of the most aggressive malignancies of the digestive system and is associated with an inferior prognosis. In recent years, its incidence has shown a trend toward younger onset. Early-onset pancreatic cancer (EOPC), defined as pancreatic cancer diagnosed at ≤ 50 years of age, has been increasing annually and may possess distinct biological and prognostic characteristics. Given the limited data from China, this study aimed to investigate the clinicopathological features and prognostic outcomes of EOPC patients.

Methods: Clinical data of 113 patients with EOPC admitted to Xiangya Hospital, Central South University, from January 2017 to December 2023 were retrospectively analyzed. Variables included demographic characteristics, clinicopathological features, and survival information. Kaplan-Meier survival curves were plotted, and differences in survival between the surgical and non-surgical groups were compared.

Results: The median age at diagnosis was 46 (42–49) years, and males accounted for 65.49% of cases. Blood type A (40.71%) and type O (34.51%) were most common. The main presenting symptoms were abdominal pain (69.91%), weight loss (62.83%), jaundice (43.36%), and abdominal distension (36.28%). Imaging findings showed bile duct dilation in 32.74%, pancreatic duct dilation in 39.82%, vascular invasion in 59.29%, and distant metastasis in 52.21% of patients. Histopathology revealed that adenocarcinoma and ductal adenocarcinoma accounted for 93.81% of all cases, with predominantly moderate or poor differentiation (76.10%). Tumors were the most frequently located in the pancreatic head (65.42%). TNM staging showed lymph node metastasis in 77.88% and stage IV disease in 52.21%. Laboratory tests demonstrated markedly elevated CA19-9 levels. Kaplan-Meier analysis indicated a median overall survival of 18.6 months for the entire cohort, with significantly longer survival in the surgical group compared with the non-surgical group (29.4 months vs. 13.8 months, $P=0.001$).

Conclusion: EOPC predominantly affects males and tends to arise in the pancreatic head. It is often diagnosed at an advanced stage or with distant metastasis and is characterized by poor differentiation and strong invasiveness. Surgical resection markedly improves survival and remains the key to prolonged prognosis. Young individuals presenting with unexplained abdominal pain, weight loss, or jaundice should be carefully evaluated through imaging to enable early diagnosis and timely surgical intervention. Future multicenter, large-sample prospective studies are warranted to validate these findings further.

Key words

Pancreatic Neoplasms; Disease Attributes; Prognosis

CLC number: R735.9

胰腺癌作为消化系统恶性程度最高的肿瘤之一，其发病率与病死率在全球范围内呈持续上升趋势^[1-2]。根据最新的文献报告，在美国胰腺癌5年生存（overall survival, OS）率仅13%^[1]，而中国最新统计结果更低，仅为8.5%^[3]，在所有癌种中OS率最低。胰腺癌的发病率随年龄增长而升高，多见于老人人群，诊断中位年龄约为70岁^[4]，因而常被视为一种老年性疾病。然而，近年来胰腺癌发病呈现出明显的年轻化趋势^[5-6]。有研究^[7]指出，在30~39岁年龄段中，胰腺癌的发病率增加了57%，增幅最为显著。目前，国内外研究多

集中于中老年患者，对早发性胰腺癌（early-onset pancreatic cancer, EOPC）的临床特征、生物学行为及预后模式的系统性研究仍较为缺乏。2007年，Sara Raimondi等^[8]首次提出将诊断时年龄低于50岁的胰腺癌定义为EOPC。EOPC已成为所有早发性癌症中增长最快的类型之一^[6]，其患病与死亡人数亦随时间迅速上升^[9]。目前多数相关研究仍以50岁作为年龄截断值^[10-11]。越来越多的证据表明，EOPC可能是一种具有独特分子特征和更强侵袭性表型的独立亚型^[10-13]，因此亟需加强对该领域的关注。然而，现有研究多基于欧美人群，中国人群

的相关数据十分有限，针对中国EOPC患者的队列研究尤为少见。本研究回顾性分析EOPC患者的临床及预后资料，旨在揭示中国EOPC人群的临床病理特征及其预后情况。

1 资料与方法

1.1 一般资料

采用回顾性队列研究方法，收集2017年1月—2023年12月在中南大学湘雅医院胰腺外科连续收治的EOPC患者病例资料。纳入标准：(1)经病理组织学诊断明确为胰腺癌；(2)诊断胰腺癌的年龄≤50岁；(3)未合并其他恶性肿瘤。排除标准：(1)胰腺神经内分泌肿瘤等其他胰腺恶性肿瘤；(2)非原发性胰腺癌；(3)病理学未明确诊断；(4)非本医院诊治的胰腺肿瘤。本研究所收集数据均为不可识别患者身份的数据，故经中南大学湘雅医院伦理审查委员会审查（审批号：2025081285），豁免患者知情同意。

1.2 观察指标及随访

收集患者的临床病理资料及随访信息，包括：年龄、性别、血型、体质质量指数(BMI)、病史等；临床表现、临床特征；术后病理资料；OS等。OS定义为从诊断到死亡日期或者最后1次随访之间的时间间隔。采用电话方式，记录患者肿瘤的生存情况。随访数据截止日期为2025年1月31日或患者死亡。

1.3 统计学处理

计数资料以绝对数[n (%)]表示；连续性计量资料中，正态分布用均数±标准差($\bar{x} \pm s$)表示，偏态分布以中位数(四分位间距)[M(IQR)]。使用Kaplan-Meier方法估计生存曲线，并通过Log-rank检验进行比较。 $P<0.05$ 为差异有统计学意义。

2 结 果

2.1 一般特征

从中南大学湘雅医院电子病历系统中筛选符合标准的EOPC患者共113例。患者年龄25~50岁，中位年龄为46(42~49)岁；男性74例(65.49%)；BMI 21.57(19.56~24.51) kg/m²。ABO血型分布以

A型(40.71%)和O型(34.51%)为主。吸烟、饮酒史以及家族史，疾病史均无特殊(表1)。

表1 EOPC患者一般特征

Table 1 Baseline characteristics of EOPC patients

资料	数值
年龄[岁,M(IQR)]	46(42~49)
性别[n(%)]	
男	74(65.49)
女	39(34.51)
血型[n(%)]	
A	46(40.71)
O	39(34.51)
B	20(17.70)
AB	4(3.54)
未查	4(3.54)
BMI [kg/m ² ,M(IQR)]	21.57(19.56~24.51)
吸烟史[n(%)]	
有	37(32.74)
无	76(67.26)
饮酒史[n(%)]	
有	24(21.24)
无	89(78.76)
糖尿病史[n(%)]	
有	7(6.19)
无	106(93.81)
肿瘤家族史[n(%)]	
有	1(0.88)
无	112(99.12)
胰腺炎病史[n(%)]	
有	2(1.77)
无	111(98.23)

2.2 临床特征

患者入院症状常表现为腹痛(69.91%)，伴随腹胀(36.28%)、黄疸(43.36%)及体质质量下降(62.83%)。影像学评估显示出现胆管扩张(32.74%)，主胰管扩张(39.82%)。此外，血管侵犯(59.29%)与脏器转移(52.21%)发生率均较高。实验室指标方面，除CA19-9明显升高外，其余肿瘤标志物与肝功能指标均无特殊(表2)。受高转移率(52.21%)影响，最终42例(37.17%)接受根治性手术(胰十二指肠切除术38例、胰腺部分切除术+脾切除术4例)。全组患者中位住院时间18(11.00~24.50)d。

表2 EOPC患者临床信息**Table 2 Clinical information of EOPC patients**

临床指标	数值
临床表现[n(%)]	
腹痛	
有	79(69.91)
无	34(30.09)
腹胀	
有	41(36.28)
无	72(63.72)
黄疸	
有	49(43.36)
无	64(56.64)
体重质量下降	
有	71(62.83)
无	42(37.17)
腹部包块	
有	9(7.96)
无	104(92.04)
压痛	
有	57(50.44)
无	56(49.56)
反跳痛	
有	4(3.54)
无	109(96.46)
临床特征[n(%)]	
胆管扩张	
有	37(32.74)
无	76(67.26)
主胰管扩张	
有	45(39.82)
无	68(60.18)
侵及血管	
有	67(59.29)
无	46(40.71)
脏器转移	
有	59(52.21)
无	54(47.79)
实验室指标[M(IQR)]	
CA19-9(KU/L)	158.50(47.99~454.10)
CA125(KU/L)	25.45(11.40~82.57)
CEA(ng/mL)	2.44(1.18~5.40)
天门冬氨酸氨基转移酶(U/L)	44.90(22.60~92.05)
丙氨酸氨基转移酶(U/L)	51.70(18.85~145.30)
直接胆红素(μmol/L)	9.10(3.85~99.35)
总胆红素(μmol/L)	19.10(10.60~168.90)
白蛋白(g/L)	40.90(37.00~44.50)

2.3 病理特征

全组肿瘤中位最大径 3.70 (2.65~4.65) cm, 其中胰头 (65.49%) 占比最多, 胰体尾 (34.51%) 次

之。组织病理诊断: 腺癌占比 47.79%, 导管腺癌占 46.02%, 其余 6.19% 为腺泡细胞癌及胰腺鳞癌等; 组织学显示低分化倾向, 高分化腺癌仅 4.43%, 中分化及低分化较多, 分别占 39.82%、36.82%。TNM 分期: T2 期 41.59%, T3 期 31.86%; 淋巴结转移 (N1+N2) 显著 (77.88%); M1 期 (AJCC IV 期) 占 52.21% (表 3)。

表3 EOPC患者临床病理特征**Table 3 Clinicopathologic characteristics of EOPC patients**

病理指标	数值
肿瘤最大径[cm,M(IQR)]	3.70(2.65~4.65)
肿瘤部位[n(%)]	
胰头	74(65.49)
胰体尾	39(34.51)
病理诊断[n(%)]	
导管腺癌	52(46.02)
腺癌	54(47.79)
其他胰腺癌	7(6.19)
分化程度[n(%)]	
高分化	5(4.43)
中分化	45(39.82)
低分化	41(36.28)
未知	22(19.47)
T分期[n(%)]	
T1	10(8.85)
T2	45(39.82)
T3	35(30.97)
T4	23(20.36)
N分期[n(%)]	
N0	25(22.12)
N1	59(52.21)
N2	29(25.67)
M分期[n(%)]	
M0	54(47.79)
M1	59(52.21)
AJCC分期[n(%)]	
I	21(18.58)
II	13(11.51)
III	20(17.70)
IV	59(52.21)

2.4 生存分析

在随访期内, 成功获取 47 例患者的完整生存数据。Kaplan-Meier 分析结果显示, 全队列中 OS 估计值为 18.60 个月 (图 1A)。根据是否进行手术治疗分组生存分析结果显示, 手术组 (n=25) OS 估计值为 29.40 个月, 非手术组 (n=22) 为 13.76 个月, 差异有统计学意义 ($P=0.0015$) (图 1B)。

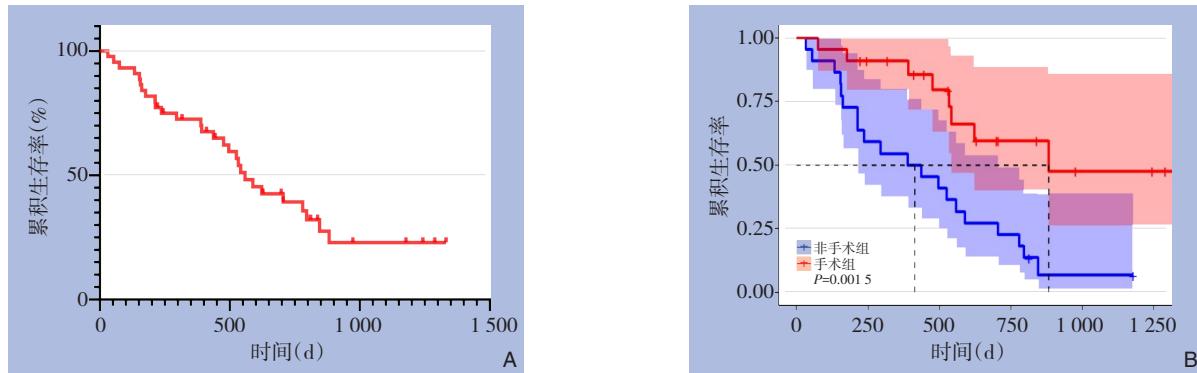


图1 EOPC患者的生存曲线

Figure 1 Survival curves of EOPC patients

A: 全组患者；B: 手术组患者 vs. 非手术组患者

A: Whole group of patients; B: Surgical group vs. non-surgical group

3 讨 论

本研究显示，EOPC 患者以男性为主（占 65.49%），这与既往研究结果一致^[5,9,14-16]。在血型分布上，本队列中 A 型血与 O 型血患者占比较高。现有证据表明，非 O 血型（尤其是 A 型）可能与胰腺癌风险增加相关^[17-18]，其潜在机制可能涉及幽门螺杆菌特异性黏附 A 抗原并诱发慢性炎症，从而促进癌变^[18-21]，但该机制在 EOPC 中的特异性仍需进一步验证。

胰腺癌早期症状隐匿且缺乏特异性，常导致诊断延迟，多数患者确诊时已处于局部进展或转移阶段，预后较差^[22-23]。虽有研究指出腹痛与黄疸是常见首发症状，而体质量下降相对少见^[22]，但本研究发现 EOPC 患者中体质量下降发生率较高，分析可能与本研究队列中 EOPC 患者转移比例较高有关。

研究表明，EOPC 生长更快、生物学行为更具侵袭性^[12,24]，肿瘤细胞增殖迅速致体积较大，更易出现局部进展或远处转移，使得部分患者确诊时已丧失手术机会。本队列中 EOPC 患者淋巴结转移（N1+N2）比例高达 77.88%，显著高于无淋巴结转移（N0）者，与基于 SEER 数据库的大样本研究^[25]结果一致。日本一项研究^[26]也显示，接受根治性手术的 EOPC 患者淋巴结转移率可达 74%。尽管与晚发性胰腺癌（late-onset pancreatic cancer, LOPC）相比，EOPC 的 N 分期差异无统计学意义（P=0.099），但其 N2 分期比例（37% vs. 25%）和病理 IV 期比例（20% vs. 7%，P=0.005）更高^[26]。淋巴结转移比例高可能与 FOXC2 在 EOPC 中上调有关，其通过增强上皮-间充质转化促进淋巴转移^[27-30]。此外，EOPC 患者远处转移及晚期病例占比较高，与国内外研究结论相符^[10,14,31]。EOPC 还呈现明显低分

化趋势，类似现象在其他研究中也观察到^[12,32-33]，其机制可能与 SMAD4 蛋白缺失更常见有关^[13,34]。SMAD4 作为 TGF-β 信号通路的关键调控因子，其缺失促进肿瘤进展、转移及预后恶化^[35-36]。

本研究结果显示，胰头是 EOPC 最常见发病部位（占 65.49%），文献^[11,37]也表明，EOPC 中胰头癌比例高于 LOPC。胰头癌易引起梗阻性黄疸及相关酶学异常，有助于较早诊断和提高手术切除率，从而改善预后^[38-39]。因此，对以黄疸为首发症状的患者应积极行影像学检查以早期识别。值得注意的是，胰体尾癌症状（如腹痛、消化不良）更为隐匿，更易发生远处转移^[40]，导致诊断延误和晚期确诊，病死率较高^[41]。

根治性手术是改善 EOPC 预后的关键。本队列 EOPC 患者的中位 OS 为 18.6 个月，其中手术组中位 OS 达 29.4 个月，明显优于非手术组的 13.8 个月。多数研究认为手术可极大改善 EOPC 预后^[26,31]，即使对于局部晚期患者，积极手术仍是合理选择^[42-43]。年轻患者一般状况好、合并症少、手术耐受性佳^[44]，因此对于 EOPC，即使分期较晚，也应采取积极态度争取根治性手术机会。

本研究为单中心回顾性研究，样本量有限，存在选择偏倚，且缺乏与 LOPC 或平均型胰腺癌的直接对照，限制了结果外推性及 EOPC 特征特异性的判断；随访数据缺失较多也影响了长期 OS 率分析的完整性；手术组与非手术组的基线特征并非完全一致，但受病例数限制，未进行倾向性评分匹配等平衡方法分析，因此两组间存在一定选择偏倚，结果可能受到混杂因素的影响，仍然需要进一步的研究验证。因此，本研究结果应视为初步探索。未来需开展多中心、大样本前瞻性研究，设立合适对照组并进行长期随访，以进一步验证

本研究结论。

综上, EOPC 具有侵袭性强、晚期比例高、低分化倾向显著的临床病理特征。根治性手术是改善预后的关键。对年轻人群出现不明原因腹痛、体质量下降或黄疸等症状时, 应提高警惕, 加强筛查, 争取早期诊断和手术机会以改善生存。

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利益冲突: 所有作者均声明不存在利益冲突。

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