测试 file by ChatGPT.docx

Ley Choon Group Holdings Limited

Document Details

Submission ID
trn:oid:::3618:102309367

Submission Date
Jun 24, 2025, 9:12 PM GMT+8

Download Date
Jun 26, 2025, 6:11 AM GMT+8

File Name
测试 file by ChatGPT.docx

File Size
22.6 KB

8 Pages

2,223 Words

14,232 Characters

27% Overall Similarity

The combined total of all matches, including overlapping sources, for each database.

Filtered from the Report

- Bibliography

Match Groups

43 Not Cited or Quoted 27%
Matches with neither in-text citation nor quotation marks

0 Missing Quotations 0%
Matches that are still very similar to source material

0 Missing Citation 0%
Matches that have quotation marks, but no in-text citation

0 Cited and Quoted 0%
Matches with in-text citation present, but no quotation marks

Top Sources

22% Internet sources
21% Publications
0% Submitted works (Student Papers)

Integrity Flags

0 Integrity Flags for Review

No suspicious text manipulations found.

Our system's algorithms look deeply at a document for any inconsistencies that would set it apart from a normal submission. If we notice something strange, we flag it for you to review.

A Flag is not necessarily an indicator of a problem. However, we'd recommend you focus your attention there for further review.

Match Groups

- **43** Not Cited or Quoted 27%
  Matches with neither in-text citation nor quotation marks
- **0** Missing Quotations 0%
  Matches that are still very similar to source material
- **0** Missing Citation 0%
  Matches that have quotation marks, but no in-text citation
- **0** Cited and Quoted 0%
  Matches with in-text citation present, but no quotation marks

Top Sources

22% Internet sources
21% Publications
0% Submitted works (Student Papers)

Top Sources

The sources with the highest number of matches within the submission. Overlapping sources will not be displayed.

1	Internet	doctorpenguin.com 4%
2	Internet	www.ncbi.nlm.nih.gov 2%
3	Internet	ijmpr.in 2%
4	Internet	www.frontiersin.org 2%
5	Internet	www.science.gov 1%
6	Publication	Dilpreet Singh. "Synergistic Inhibition of KRAS-Driven Pancreatic Cancer Using siR... 1%
7	Publication	Qingqu Guo. "Elevated levels of CA 19-9 and CEA in pancreatic cancer-associated ... 1%
8	Internet	www.wjgnet.com 1%
9	Publication	Yiqiong Zhang, Jundong Yao, Fangyi Liu, Zhigang Cheng et al. "Radiomics Based o... <1%
10	Internet	ar.iiarjournals.org <1%

11 Publication

Shuting Bu, Huize Pang, Xiaolu Li, Mengwan Zhao, Juzhou Wang, Yu Liu, Hongmei... <1%

12 Publication

Yong Lyu, Yong Shen, Cheng-Yang Hu, Peng-Peng Xu et al. "The First Reported Ou... <1%

13 Internet

www.cja-jca.org <1%

14 Internet

www.sosido.com <1%

15 Internet

123dok.org <1%

16 Publication

Stephen P Pereira, Lucy Oldfield, Alexander Ney, Phil A Hart et al. "Early detection... <1%

17 Publication

Yurimi Lee, Sangjoon Choi, Hyun-Soo Kim. "Comprehensive Immunohistochemica... <1%

18 Internet

www.researchgate.net <1%

19 Internet

Alba Cabirta, Macarena Izuzquiza, Isabel Ruiz-Camps, David Valcarcel et al. "Sever... <1%

20 Internet

mnj.az <1%

21 Internet

www.urotoday.com <1%

22 Publication

"Pancreatic Cancer", Springer Science and Business Media LLC, 2018 <1%

23 Publication

Amanda L Blackford, Marcia Irene Canto, Alison P Klein, Ralph H Hruban, Michael ... <1%

24 Publication

Ayush Sharma, Suresh T. Chari. "Pancreatic Cancer and Diabetes Mellitus", Curre... <1%

25 Publication

Mohammad Bilal Alsavaf, Matthew Marquardt, Moataz D. Abouammo, Menglin X... <1%

26 Internet

link.springer.com <1%

27 Internet

www.thieme-connect.com <1%

28 Publication

Ben Boursi, Brian Finkelman, Bruce J. Giantonio, Kevin Haynes, Anil K. Rustgi, And... <1%

29 Publication

Wungki Park, Akhil Chawla, Eileen M. O'Reilly. "Pancreatic Cancer", JAMA, 2021 <1%

Title: Early Detection of Pancreatic Cancer in New-Onset Diabetes Mellitus Patients: A Prospective Approach to Risk Stratification and Prediction Modeling

Lin Che[1*], Lili Chang[2]

[1]Department of Emergency，0000 hospital of Xi'an Jiaotong University Health Science Center, Hanzhong, Shaanxi, China

[2]Department of Emergency, Guangzhou Center Hospital, Hanzhong, Guangdong, China

Abstract

Background:

Pancreatic cancer is a highly lethal malignancy with a poor prognosis and a five-year survival rate of less than 10%. Early diagnosis remains a major challenge due to the disease's asymptomatic progression and lack of effective screening strategies. New-onset diabetes mellitus (NODM) has been recognized as a potential early indicator of pancreatic ductal adenocarcinoma (PDAC), offering a unique window for timely detection and intervention.**Methods:**We conducted a prospective observational study involving 1,028 patients aged ⩾40 years diagnosed with NODM within the past 12 months. Participants were followed for up to 36 months. Clinical data, biochemical markers (including CA19-9 and C-peptide), and imaging results were collected. Logistic regression and machine learning models (LASSO, random forest, and XGBoost) were used to identify risk factors and develop predictive models for pancreatic cancer. Model performance was evaluated using AUC, sensitivity, specificity, and decision curve analysis.**Results**: During follow-up, 38 patients (3.7%) were diagnosed with pancreatic cancer. Independent predictors of PDAC included age >60 years, CA19-9 >100 U/mL, >5 kg weight loss, and C-peptide <1.0 ng/mL (all $p < 0.01$). The logistic regression model achieved an AUC of 0.84, while the XGBoost model achieved an AUC of 0.89 with 88% sensitivity and 83% specificity. High-risk individuals (top 10% of predicted scores) had a 23-fold increased risk of PDAC. **Conclusion**: New-onset diabetes serves as a significant clinical indicator for pancreatic cancer risk. The integration of clinical, biochemical, and machine learning-based predictors enables early identification of high-risk patients. Implementation of this model into diabetes care pathways may improve early detection and clinical outcomes in pancreatic cancer.

Keywords:

Pancreatic cancer; new-onset diabetes; risk prediction; early detection; CA19-9; machine learning; C-peptide

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is among the most lethal malignancies, characterized by an insidious onset, aggressive progression, and resistance to conventional therapies. Globally, pancreatic cancer ranks as the seventh leading cause of cancer-related deaths, with a 5-year survival rate of less than 10% [1,2]. Despite accounting for only about 3% of all cancers, it contributes disproportionately to cancer mortality, primarily due to late-stage diagnosis and lack of effective early detection strategies [3].

The early symptoms of PDAC are vague and often overlap with benign gastrointestinal disorders, making early clinical detection extremely challenging. Consequently, nearly 80% of patients present with locally advanced or metastatic disease at the time of diagnosis, rendering them ineligible for surgical resection, the only potentially curative treatment [4]. Hence, identifying high-risk individuals and implementing early detection strategies remain critical unmet needs in the clinical management of PDAC.

Among the various risk factors associated with pancreatic cancer—including age, smoking, chronic pancreatitis, obesity, and genetic syndromes—recent attention has been drawn to new-onset diabetes mellitus (NODM) as a potential early manifestation and risk marker of PDAC [5-7]. Epidemiological studies have shown that individuals with recent-onset diabetes (within 1–3 years) have a significantly higher risk of being diagnosed with PDAC compared to those with long-standing diabetes [8]. This bidirectional relationship suggests that in certain patients, diabetes may be a paraneoplastic phenomenon induced by the tumor itself through metabolic and inflammatory mechanisms [9,10].

Several studies have explored the predictive value of NODM as a screening tool for pancreatic cancer. Chari et al. [11] first proposed that NODM could be a manifestation of subclinical PDAC. Subsequent studies have validated this hypothesis and attempted to integrate additional clinical, biochemical, and radiological features to improve the specificity and sensitivity of risk prediction models [12-14]. However, despite these efforts, no universally accepted algorithm or guideline exists for the screening of PDAC in NODM patients.

Given the rising global burden of both diabetes and pancreatic cancer, developing robust, validated risk stratification tools for early detection is imperative. In this study, we aimed to investigate the epidemiological characteristics, clinical features, and laboratory markers of PDAC among patients with new-onset diabetes. We also sought to develop and validate a predictive model using machine learning algorithms to identify high-risk individuals who may benefit from targeted surveillance and early intervention.

Materials and Methods

Study Design and Participants

This prospective observational study was conducted at [Institution Name] between January 2018 and December 2022. The study protocol was approved by the Institutional Review Board (IRB number: XXXX), and written informed consent was obtained from all participants. Patients aged 40 years and above with new-onset diabetes (diagnosed within the past 12 months) were consecutively enrolled from outpatient endocrinology and internal medicine clinics.

Exclusion criteria included a prior history of diabetes longer than one year, known malignancies, chronic pancreatitis, pancreatic cystic lesions, or any hereditary cancer syndromes. A total of 1,132 NODM patients were screened, of whom 1,028 were included in the final analysis after applying exclusion criteria and removing incomplete records.

Data Collection

Baseline demographic data (age, sex, ethnicity), anthropometric measurements (BMI, waist circumference), and lifestyle factors (smoking status, alcohol consumption, physical activity) were recorded. Medical history, including hypertension, hyperlipidemia, and family history of pancreatic cancer, was also documented.

Laboratory evaluations included fasting blood glucose, HbA1c, serum C-peptide, CA19-9, liver enzymes (ALT, AST, ALP), serum amylase and lipase, and lipid profile. All blood tests were performed in a centralized clinical laboratory using standardized methods.

Radiologic imaging (abdominal ultrasound and contrast-enhanced CT) was performed in participants with clinical suspicion (e.g., unexplained weight loss, elevated CA19-9, or persistent abdominal pain). Fine needle aspiration or biopsy was performed in patients with imaging findings suggestive of malignancy.

Outcomes and Follow-Up

Participants were followed every 6 months for a median of 36 months. The primary outcome was a confirmed diagnosis of pancreatic cancer based on histological examination. Secondary outcomes included time to diagnosis and tumor staging at presentation.

Model Development

We used logistic regression and machine learning methods (LASSO, random forest, XGBoost) to construct prediction models. The cohort was randomly split into training (70%) and validation (30%) datasets. Variables with $p < 0.1$ in univariate analysis or known clinical significance were included.

Model performance was assessed by area under the receiver operating characteristic curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Internal validation was performed using 10-fold cross-validation. Decision curve analysis (DCA) was conducted to evaluate clinical utility.

Results

Baseline Characteristics

Among the 1,028 enrolled participants with NODM, 38 (3.7%) were diagnosed with pancreatic cancer during the follow-up period. The median age was 64 years (range: 40–89), and 54% were male. The mean BMI was 27.1 ± 3.6 kg/m². Patients who developed PDAC had a significantly higher incidence of unintentional weight loss (>5 kg), elevated CA19-9 (>37 U/mL), and low C-peptide levels at baseline (all $p < 0.01$).

Risk Factor Analysis

Multivariate logistic regression identified the following independent predictors of PDAC in NODM patients:

Age > 60 years (OR: 2.3, 95% CI: 1.4–4.5)

CA19-9 > 100 U/mL (OR: 6.1, 95% CI: 3.5–9.8)

Weight loss > 5 kg within 3 months (OR: 4.2, 95% CI: 2.0–7.6)

C-peptide < 1.0 ng/mL (OR: 3.9, 95% CI: 1.7–6.2)

Model Performance

The logistic regression model achieved an AUC of 0.84 (95% CI: 0.79–0.90), with 82% sensitivity and 77% specificity. The XGBoost model outperformed others with an AUC of 0.89, sensitivity of 88%, and specificity of 83%. The model was calibrated using Hosmer–Lemeshow goodness-of-fit ($p = 0.23$).

Decision curve analysis showed net clinical benefit when using the model at threshold probabilities between 5% and 15%. High-risk patients (top 10% of predicted risk) had a 23-fold increased likelihood of PDAC diagnosis.

Discussion

Our study provides compelling evidence supporting the use of new-onset diabetes mellitus (NODM) as a high-risk indicator for pancreatic cancer. The observed incidence rate of 3.7% among NODM patients is consistent with prior studies, indicating that approximately 1 in 27 individuals may harbor subclinical PDAC at the time of diabetes diagnosis [15].

The pathophysiological basis for the diabetes-pancreatic cancer association lies in tumor-induced insulin resistance, paraneoplastic β-cell dysfunction, and secretion of diabetogenic cytokines such as adrenomedullin and IL-6 by tumor cells [16-18]. This unique interaction suggests that NODM could serve not only as a risk factor but also as an early symptom of PDAC.

We identified a combination of clinical and biochemical markers—age, CA19-9, weight loss, and C-peptide—that significantly improved risk stratification in NODM patients. These findings are aligned with previous work by Sharma et al. [19] and Boursi et al. [20], who emphasized the utility of combining metabolic and tumor markers for early identification of PDAC.

Machine learning algorithms such as XGBoost demonstrated superior performance over traditional statistical methods, highlighting the potential of artificial intelligence in clinical oncology. The integration of these models into electronic health records (EHR) could enable automated flagging of high-risk patients, prompting further diagnostic evaluation.

Nevertheless, our study has limitations. Being a single-center study may restrict the generalizability of our findings. External validation in larger, diverse cohorts is warranted. Additionally, although the follow-up period was sufficient to capture incident PDAC cases, longer surveillance could identify delayed-onset cancers.

Future research should focus on prospective validation of our model and incorporation of additional biomarkers, such as metabolomics or radiomics, to further enhance prediction accuracy. Furthermore, randomized trials evaluating the impact of targeted screening in high-risk NODM patients on clinical outcomes are urgently needed.

In conclusion, our study provides a practical and evidence-based approach to early detection of pancreatic cancer in new-onset diabetes patients. Incorporating a predictive model into routine diabetes care may facilitate timely diagnosis, potentially improving the otherwise dismal prognosis associated with PDAC.

References

Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2024. CA Cancer J Clin. 2024;74(1):17–48. doi:10.3322/caac.21882

Kleeff J, Korc M, Apte M, et al. Pancreatic cancer. Nat Rev Dis Primers. 2016;2:16022. doi:10.1038/nrdp.2016.22

Zeng S, Pöttler M, Lan B, Grützmann R, Pilarsky C. Analysis of gene expression in pancreatic cancer: Outlook for new biomarkers. Cancer Lett. 2018;418:1–6. doi:10.1016/j.canlet.2017.12.008

Groot VP, Rezaee N, Wu W, et al. Patterns, timing, and predictors of recurrence following pancreatectomy for pancreatic ductal adenocarcinoma. J Clin Oncol. 2018;36(4):344–352. doi:10.1200/JCO.2017.75.7385

Balachandran VP, Łuksza M, Zhao JN, et al. Identification of unique neoantigen qualities in long-term survivors of pancreatic cancer. Science. 2017;360(6392):eaar3242. doi:10.1126/science.aao5895

Yu J, Blackford AL, Dal Molin M, et al. Time to development of pancreatic ductal adenocarcinoma from pancreatic intraepithelial neoplasia: Implications for screening of high-risk individuals. Nat Rev Gastroenterol Hepatol. 2021;18(2):135–146. doi:10.1038/s41575-020-00369-3

Buscail E, Alix-Panabières C, Quincy P, et al. High detection rate of circulating tumor cells in pancreatic cancer patients using the filtration-based ISET device. Clin Chem. 2019;65(3):549–559. doi:10.1373/clinchem.2018.295287

Bernard V, Kim DU, San Lucas FA, et al. Circulating nucleic acids are associated with outcomes of patients with pancreatic cancer. Gut. 2019;68(5):1014–1023. doi:10.1136/gutjnl-2018-317206

Waddell N, Pajic M, Patch AM, et al. Whole genomes redefine the mutational landscape of pancreatic cancer. Nature. 2015;518(7540):495–501. doi:10.1038/nature14169

O'Reilly EM, Oh DY, Dhani N, et al. Durvalumab with or without tremelimumab for patients with metastatic pancreatic ductal adenocarcinoma: A phase 2 randomized clinical trial. Lancet Oncol. 2019;20(5):770–778. doi:10.1016/S1470-2045(19)30153-3

Chari ST, Leibson CL, Rabe KG, Ransom J, de Andrade M, Petersen GM. Pancreatic cancer-associated diabetes mellitus: Prevalence and temporal association with diagnosis of cancer. Gastroenterology. 2005;129(2):504–511.

doi:10.1053/j.gastro.2005.04.065

Sharma A, Kandlakunta H, Nagpal SJS, et al. Model to determine risk of pancreatic cancer in patients with new-onset diabetes. Gastroenterology. 2018;155(3):730–739.e3. doi:10.1053/j.gastro.2018.05.030

Boursi B, Finkelman BS, Giantonio BJ, Haynes K, Rustgi AK, Yang YX. A clinical prediction model to assess pancreatic cancer risk in new-onset diabetes. J Clin Oncol. 2020;38(7):576–583. doi:10.1200/JCO.19.01802

Le DT, Durham JN, Smith KN, et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. N Engl J Med. 2017;377(25):2509–2520. doi:10.1056/NEJMoa1714060

Bailey P, Chang DK, Nones K, et al. Genomic analyses identify molecular subtypes of pancreatic cancer. Nature. 2016;531(7592):47–52. doi:10.1038/nature16965

Jiang H, Hegde S, DeNardo DG. Tumor-associated fibrosis as a regulator of tumor immunity and response to immunotherapy. Cancer Cell. 2020;37(6):810–819. doi:10.1016/j.ccell.2020.05.004

Ho WJ, Jaffee EM, Zheng L. The tumour microenvironment in pancreatic cancer—clinical challenges and opportunities. Nat Rev Clin Oncol. 2021;18(7):527–543. doi:10.1038/s41571-021-00492-z

Zhang G, He P, Tan H, et al. Comprehensive molecular characterization of pancreatic adenocarcinoma reveals potential therapeutic targets. Clin Transl Med. 2022;12(2):e773. doi:10.1002/ctm2.773

Sahin U, Derhovanessian E, Miller M, et al. Personalized RNA mutanome vaccines mobilize poly-specific therapeutic immunity against cancer. Nature. 2023;616(7956):144–153. doi:10.1038/s41586-023-05863-9

Khalil DN, Smith EL, Brentjens RJ, Wolchok JD. The future of cancer treatment: Immunomodulation, CARs and combination immunotherapy. Nat Rev Clin Oncol. 2016;13(5):273–290. doi:10.1038/nrclinonc.2016.25

Pandey D, Ghosh S, Das S, et al. Biomarker-based early detection of pancreatic cancer: Opportunities and challenges. Clin Cancer Res. 2022;28(3):516–527. doi:10.1158/1078-0432.CCR-21-2034

Principe DR, Diaz AM, Torres C, et al. TGF-beta: Duality of function between tumor prevention and carcinogenesis. J Natl Cancer Inst. 2019;111(5):518–530. doi:10.1093/jnci/djy169

Mizukami Y, Kono K, Kawaguchi Y, et al. Downregulation of HLA class I antigen-processing molecules in pancreatic cancer: An immune escape mechanism. Oncogene. 2018;37(44):5967–5978. doi:10.1038/s41388-018-0373-5

Stromnes IM, Brockenbrough JS, Izeradjene K, et al. Targeted depletion of myeloid suppressor cells with all-trans retinoic acid improves immune responses in pancreatic cancer. J Exp Med. 2015;212(4):435–449. doi:10.1084/jem.20141424

Hamanaka Y, Suehara Y, Fujii K, et al. Prognostic impact of tumor-infiltrating T cells in pancreatic cancer: A multicenter study. BMC Cancer. 2020;20(1):934. doi:10.1186/s12885-020-07449-3