Abstract

The Center for Disease Control and Prevention estimates that instances of pancreatic cancer (PC) have increased over 60% from 2000 to 2017(1). With only about 4% of patients surviving 5 years after diagnosis, PC is one of the most deadly forms of cancer (13). Artificial intelligence is an increasingly prevalent form of technology that allows for the creation of computer models that can predict and learn. This review considered the existing literature relevant to the applications of artificial intelligence to PC and found 3 major trends: the use of AI to differentiate chronic pancreatitis (CP) from PC, risk assessment of PC, and the early diagnosis of PC. Additionally, less popular applications are considered.

Introduction

The American Cancer Society predicts that over 57,000 people will be diagnosed with pancreatic cancer (PC) and over 47,000 will die of the disease in 2020 (4). PC occurs when the DNA in the nuclei of pancreatic cells undergo mutation, making them unable to respond to normal biological cues (13). As a result, they proliferate unchecked, creating tumors that can become malignant and metastatic. With only about 4% of patients surviving 5 years after diagnosis, PC is one of the most deadly forms of cancer (13). The Center for Disease Control and Prevention estimates that instances of PC have increased over 60% from 2000 to 2017 (1). As this disease continues to harm more individuals, it is imperative to find ways to mitigate the effects of this malady.

One efficient means of tackling this problem is artificial intelligence, algorithms capable of performing learning and problem-solving tasks. Specifically, the use of Convolutional Neural Networks (CNN's) has been continuously on the rise. CNN's are a powerful tool primarily employed by AI visualization tasks. Composed of numerous computing units or "neurons", these algorithms can be programmed to extract characteristic features from images in order to classify them (10). This makes them the computational method of choice for categorizing data based on the CT scans, MRI scans, etc abundant in medicine. As a result, it follows that use of CNN's may be useful for the prevention and early diagnosis, among other applications, of pancreatic cancer.

Methods

To locate articles for review, I utilized the publicly available National Center for Biotechnology Information, Science Direct, and Brown University Library search tools. These databases allowed the study to access published articles of pancreatic cancer

related reviews and studies. The key words used to narrow search criteria were “artificial intelligence”, “pancreatic cancer”, “early detection/diagnosis”, “machine learning”, and “computational biology”. After relevant articles were located, they were read with their methods and results recorded for review. Studies were grouped by their specific applications of machine learning and inferences were made according to findings.

Results

Upon researching for articles, it soon became apparent that there was not a plethora of literature on AI and PC at the time of the conduct of this review. However, there were a fair amount of articles detailing different approaches that were in need of a larger contextualization that the single existing review could not provide, hence the utility of this study. It became clear that the existing research fell into three main categories in order of the greatest to least number of articles available on the subject: differentiation of CP from PC, risk assessment of PC, and diagnosis of PC. Accordingly, the Conclusion section of this article organizes findings by these groups. Below is a table summary of the existing literature on AI and pancreatic cancer.

Table 1: Summarization of Studies

Study	Grouping	Method	Results
2	Differentiation of CP from PC	ANN	Area under curve: 0.93
4	Differentiation of CP from PC	ANN	Accuracy: 92%, 88.5%, and 91.7%, respectively; Sensitivity: 87.5%, 85.7%, and 93.3%, respectively; Specificity: 94.1%, 91.7%, and 88.9%, respectively
8	Differentiation of CP from PC	MNN	Testing accuracy: 95%
9	Differentiation of	ANN	Sensitivity: 94.64%;

	CP from PC		Specificity: 94.44%
13	Differentiation of CP from PC	SVM	Sensitivity: 94.2%; Specificity: 96.25%
1	Risk evaluation of PC	CNN	Sensitivity: 92%; Specificity: 52%
7	Risk evaluation of PC	ANN	(Training and testing respectively) Sensitivity: 87.3 and 80.7% Specificity of 80.8 and 80.7%
12	Risk evaluation of PC	RadSTM-ER	Area under the curve: 0.8951; Accuracy of 85.19% Sensitivity: 88.89%; Specificity: 77.78%,
3	Diagnosis	ANN	Under area the curve: 0.966, Sensitivity: 95.7%; Specificity, 91.9%; Accuracy: 92.9%
5	Diagnosis	R-CNN	Area under curve: 0.9632
6	Diagnosis	K-means, MNN	Accuracy (benign vs malignant):100% Accuracy (atypical): 77%
11	Diagnosis	SVM, LDM-RFE	Biomarkers found: 7

Conclusions

Differentiating Chronic Pancreatitis from Pancreatic Cancer

Of the 13 studies included in the review, 5 were concerned with using CAD to differentiate CP from PC. Additionally, most of these studies used endoscopic ultrasound (EUS) images as data. Indeed, similar approaches were used; Das (3), Kurt (6), Săftoiu(12), and Săftoiu(10) all utilized Artificial Neural Networks (ANN) in some shape or form, while study 2 used a Support Vector Machine (SVM). Das considered how accurately CAD could be used to extract image parameters from EUS images (3). This was fairly successful, with sensitivity and specificity reported as 94.2% and 96.25% respectively. As the authors noted, their model is “highly accurate, [and] non invasive”. Kurt utilized an ANN after Principal Component Analysis (PCA) was performed to reduce the complexity of the EUS images (6). This model attained an area under the curve of 0.93. Study 9 has similarly attractive results, although it followed a markedly different setup, splitting the data into three Regions of Interests (ROI) with groups <40, 40-60, and 60< years old. An ANN was used and the results found that when age groups were tested separately, the model performed better; the accuracy of the <40, 40-60, and 60< years old groups were 92%, 88.5%, and 91.7%, respectively. Similarly their sensitivities were 87.5%, 85.7%, and 93.3%, respectively and their specificities were 94.1%, 91.7%, and 88.9%, respectively. Săftoiu sought to confirm the validity of parameters derived from time-intensity curve (TIC) analysis (12). The ANN trained to do so achieved a sensitivity of 94.64% and a specificity of 94.44% The fourth study was a cross-sectional feasibility study; its objective was to check the validity of real-time EUS elastography (an imaging processing procedure). Hue histograms were created for each individual image ,each of which were subject to “an extended neural network analysis” (10). The multilayer perceptron neural network (MNN) trained on this data achieved a testing performance of 95%. As these studies have shown, it is clear that the differentiation of CP from PC in EUS images and beyond is a well explored area with accurate models. In the future, researchers should vary the range of imaging data used and further refine the area of focus as study 9 accomplished by creating ROI’s. However, due to the overwhelming success of these six models, it would not be incorrect for the ANN’s to advance to clinical trials for implementation in widespread healthcare.

Diagnosis of Pancreatic Cancer

There are several uses of AI for the diagnosis of PC. Studies Momeni-Boroujeni (8), Liu (7), Kurita (5), and Wang (14) investigate this. The first study used Fine-Needle Aspiration (FNA) biopsy cell cluster images as data (8). The K-means algorithm was utilized to separate the cells into ROI’s to make feature extraction easier. Finally, an MNN trained on this data was found to be 100% accurate in distinguishing benign from

PC and 77% accurate for “atypical” data, suggesting promising clinical applications to inconclusive images. Liu used a Faster Region-Based Convolutional Network (R-CNN). The study utilized CT image data and achieved an area under the curve of 0.9632 (7). The authors also noted that it took 0.2 seconds for the Faster R-CNN to process an image, significantly quicker than any imaging specialist. Kurita analyzed cyst fluid to distinguish PC from benign lesions (5). The ANN attained an area under the curve of 0.966 with accuracy, sensitivity, and specificity being 92.9%, 95.7%, and 91.9%. The study also compared the diagnostic ability of carcinoembryonic antigen (CEA) and cytology to that of the model, finding that the ANN’s accuracy was greater than that of CEA ($p<0.001$) and cytology ($p=0.210$). Lastly, Wang sought to use the Support Vector Machine Recursive Feature Elimination (SVM-RFE) and Large Margin Distribution Machine Recursive Feature (LDM-RFE) algorithms to predict potential biomarkers for PC (14). The study utilized the GSE15471 dataset from the Gene Expression Omnibus repository. The study offered 7 gene markers, 3 of which were found to code for proteins that could be potentially relevant for PC diagnosis, according to their verified biological ties to urinary excretion. Regarding the use of AI for the diagnosis of PC, current research varies greatly in approach. In order for these results to be made clinically significant, it is important for more research to be conducted that utilizes similar data and machine learning methods as previous studies in order to confirm results.

Risk Assessment of Pancreatic Cancer

The second most published use of AI in PC is for risk assessment. Muhammad (9), Corral (2), and Zhou (15) all utilized ML in some shape or form for the purpose of predicting the risk of PC. Muhammad utilized an ANN trained on the National Health Interview Survey (NHIS) and Pancreatic, Lung, Colorectal, and Ovarian Cancer (PLCO) datasets (9). The resulting ANN’s training and testing sensitivities were 87.3 and 80.7%, and specificities 80.8% and 80.7%, respectively. As the authors postulated, this would make it easier to identify high-risk individuals in the larger population. The goal of Corral’s study was to use deep learning to identify pancreatic lesions (using MRI images of intraductal papillary mucinous neoplasms) that have a high probability of developing into PC (2). Using a CNN, their model was able to achieve moderate success with a sensitivity and specificity of 92% and 52%, respectively, to detect dysplasia. However, their model worked better on high-grade dysplasia/cancer, achieving a sensitivity and specificity of 75% and 78% respectively. Zhou used a “RadSTM-ER” (a binary classifier hybrid of a support tensor machine and evidence reasoning technique) and CT scans to predict the development of PC (15). The resulting model achieved an area under the curve, accuracy, sensitivity, and specificity of 0.8951, 85.19%, 88.89%, and 77.78%

respectively, indicating effectiveness. Overall, in consideration of the small number of publishings on AI for PC risk assessment and the moderate success of the ML algorithms, this area should be explored further. More studies should be conducted with a stronger focus on using publically available data; both these explorations of AI in PC risk assessment and CP-PC differentiation utilized medical imaging methods extensively. If cost and labor efficient ways to predict outcomes from publicly available databases were feasible, like those utilized in Muhammad's study (9), they would likely be cheaper than many forms of medical imaging. It is clear that more research should be conducted on this subject area.

It is apparent that there are three distinct applications of AI to PC; differentiating between CP and PC, evaluating the risk of PC, and diagnosing PC. Among the three, the models that perform differentiation between CP and PC, especially those trained on EUS images, have made the most progress in terms of both quantity of research available and model statistics. These models are ready for the preliminary stages of clinical implementation. Evaluation of the risk and the diagnosis of PC require more research. Specifically, future studies on the evaluation of risk of PC have room to improve on sensitivity and specificity among other test statistics as the current models don't perform well enough. Additionally, diagnostic methods for PCs have a wide range of methods for so little a conglomeration of papers. This lack of consistency makes replication imperative before any models are implemented in the clinic; sound results must first be obtained. Overall, in hopes for a future with AI integrated effectively in our healthcare system, it is important for more research to be conducted on the intersection of AI and PC.

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