Prognostic factors of the survival of pancreatic cancer patients in peninsular Malaysia: A survival analysis

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ABSTRACT

Introduction: Pancreatic cancer incidence in Malaysia is steadily on the rise, now ranking as the 14th most common malignancy in the country. Despite this upward trend, research on prognostic factors affecting pancreatic cancer survival remains limited, highlighting the need for ongoing investigation to improve patient survival outcomes.

Materials and Methods: This study was conducted retrospectively by reviewing records of pancreatic cancer patients hospitalized between January 2011 and December 2018 across multiple health centres in Malaysia. Using Cox proportional hazards regression analysis, several prognostic factors were identified.

Results: The study revealed that being Chinese, having a family history of pancreatic cancer, having hepatitis C, presenting with jaundice, experiencing pale stools, having a palpable mass in the abdomen, the presence of ascites, receiving palliative care and end-of-life care were associated with higher mortality risk. Conversely, being female, having hypertension, and higher haemoglobin levels were linked to decreased mortality risk.

Conclusions: These study findings offer valuable insights into prognostic factors for predicting patient outcomes and optimizing individual prognosis in pancreatic cancer cases within Malaysia context. Future research should build on these findings, exploring how these factors can be integrated into comprehensive care plans that address the specific needs of diverse patient populations.

KEYWORDS:
Pancreatic cancer, prognostic factors, Cox regression, survival, Malaysia, retrospective record review

INTRODUCTION

Pancreatic cancer has become as an emerging non-communicable disease, manifesting a gradual escalation in its incidence over recent years. Currently ranked as the 12th most common oncological disease globally,[1] its prevalence is rising by 1.1% annually.[2] Understanding its potential risk factors and recognizing its signs and symptoms are of ultimate importance for primary prevention and early diagnosis of the disease. However, pancreatic cancer is often clinically silent, and patients are frequently diagnosed at advanced stages. Consequently, its survival rate is exceedingly low compared to other malignancies.[3] In the year 2020, the disease was responsible for 466,003 global fatalities,[4] nearly matching the number of new cases annually.[2] Pancreatic cancer fatalities contribute to 4.7% of all global cancer-related deaths, making it the seventh leading cause of cancer mortality among all oncological diseases.[4]

Prognosis in pancreatic cancer patients depends on several factors. Prognostic factors are variables that indicate which patients are likely to do better or worse over time. Data on prognostic factors provide insights on the natural history of a disease, and these data are crucial to predict patients' probable outcomes and optimise patient individual's prognosis.[5] In Malaysia, the incidence of pancreatic carcinoma is on the rise, with reported cases increasing from 976 in 2018[6] to 1089 in 2020,[7] representing the 14th most common malignancy in the country.[7] Despite this upward trend, research on prognostic factors affecting survival of pancreatic cancer patients in Malaysia remains limited. A comprehensive understanding and identification of these factors are imperative for effective management. To date, the prognostic factors of pancreatic carcinoma are still insufficiently known. Therefore, ongoing research aimed at elucidating prognostic factors and improving survival rates for pancreatic cancer patients is essential. This study aims to provide further insights into the influencing factors on the overall survival of pancreatic cancer patients through a multicentre retrospective cohort study in Malaysia.

MATERIALS AND METHODS

A retrospective cohort study was conducted by comprehensively reviewing the medical records pertaining to pancreatic cancer patients aged 18 years and above, who were admitted to State hospitals in Terengganu, Kelantan, Penang, and Kedah between January 2011 and December 2018. Inclusion criteria encompassed patients with confirmed pancreatic cancer diagnoses, established through histopathology examination or various diagnostic imaging modalities. Patients with incomplete medical records exceeding 30% and those diagnosed with secondary pancreatic cancer were excluded from the study.

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The event in this study was pancreatic cancer cases who died from pancreatic cancer, and their survival time was defined as the duration in months from the date of diagnosis to the date of death. For censored cases and individuals lacking information on the date of expiry, survival time was calculated from the date of diagnosis to the last-recorded follow-up date. All relevant and eligible data were collected utilizing a constructed proforma. Treatment modalities included surgical resection followed by adjuvant therapy, palliative care and end-of-life care. Anticipating a potential 10% rate of missing values, the study aimed for a total sample size of 335 patients. Details regarding its sample size calculation and the proforma except blood test results have been previously published elsewhere.[8]

The statistical analysis was performed using statistical software for data science (STATA) version 17.0.[9] The data was evaluated using descriptive statistics and Cox regression analysis. Quantitative variables were summarized with mean and standard deviation (SD), while qualitative variables were presented as counts and percentages. For the univariable analysis step of survival analysis, simple Cox regression was utilized to identify potential prognostic factors. Covariates with a significance level (p-value) of 0.25 or lower were selected for inclusion in subsequent multivariable modelling.

Multiple Cox proportional hazards regression was then employed to determine the prognostic factors of the malignancy. $p<0.05$ was considered statistically significant. The parsimonious model, incorporating the fewest significant variables, resulting from the forward stepwise selection method, was chosen in this study. Next, the linearity of continuous variables was assessed using the multivariable fractional polynomials approach via the Fracpoly command. Multicollinearity was then evaluated through a comprehensive examination of the correlation matrix, variance inflation factor (VIF) and tolerance tests. Subsequently, potential two-way biologically or clinically meaningful interaction terms between significant independent variables were evaluated.

After that, the model's specification error was examined using the link test, while the proportional hazard assumptions were evaluated both graphically and through mathematical approach such as the scaled and unscaled Schoenfeld tests and C-statistics. As for model adequacy assessment, regression diagnostic statistics such as checking Martingale residuals, Cox-Snell residuals, deviance residuals and influence analysis were performed. Remedial measures were applied for the influential observations detected from the regression diagnostics. Any observations having regression coefficient changes of more than 20% were deleted from the model.

Final results were presented with both crude and adjusted hazard ratios, accompanied by 95% confidence intervals (95% CI), and their corresponding p-values. The study protocol and ethical aspects were approved by Universiti Sultan Zainal Abidin Human Research Ethics (UHREC) (Study protocol code: UniSZA/UHREC/2020/169) and the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia (NMRR-20-1339-52843 (IRR)).

RESULTS

Between 2011 and 2018, the medical records of total 376 pancreatic cancer patients could be retrieved. Detailed information on these patients, including their baseline characteristics, lifestyle, family cancer history, comorbidities, signs and symptoms at diagnosis, pathological findings, and treatment methods, has been reported previously elsewhere.8 Among the haematological variables, haemoglobin values could be retrieved for only 359 patients. The mean haemoglobin level among pancreatic cancer patients was found to be 12.86 g/dL (SD=1.23). Due to missing values exceeding 30% for other laboratory parameters, those variables were excluded from the analysis.

The potential significant survival predictors of pancreatic cancer were identified by means of simple Cox proportional regression analysis. Considering no other confounding variables, the results of univariable analysis revealed several factors associated with increased risk of mortality among pancreatic cancer patients. These factors included age 60 years and above, female patients (HR: 0.78; 95%CI: 0.57, 1.06), Chinese ethnicity (HR: 1.40; 95%CI: 1.02, 1.91), being married, being widowed or divorced, having history of smoking, alcohol consumption, having family history of pancreatic cancer (HR: 1.39; 95%CI: 0.89, 2.18), comorbidities such as pancreatitis, type II diabetes, hepatitis C (HR: 2.17; 95%CI: 1.01, 4.64), cirrhosis, hypertension (HR: 1.36; 95%CI: 0.99, 1.87), and ischemic heart disease.

Additionally, symptoms at presentation such as abdominal pain, back pain, loss of appetite, fatigue, nausea and vomiting, jaundice (HR: 8.27; 95%CI: 5.67, 12.06), lack of colour in faeces (HR: 7.07; 95%CI: 4.31, 11.60), dark colour urine, fever, abdominal distension, dyspepsia, presence of mass in abdomen (HR: 4.35; 95%CI: 2.72, 6.94) along with haemoglobin levels (HR: 0.40; 95%CI: 0.34, 0.47) were found to significantly impact survival. Furthermore, diagnosed with neuroendocrine tumours, location of tumour at body, receiving palliative treatment (HR: 1.92; 95%CI: 1.25, 2.95) or best supportive care (HR: 14.82; 95%CI: 9.12, 24.10), hepatomegaly and ascites (HR: 6.74; 95%CI: 4.10, 11.09) demonstrated potential effect on survival of the patients.

In the final model after removing two influential observations, several variables were found to be significant prognostic factors for the pancreatic cancer patients' survival. These variables included being female (HR: 0.11; 95%CI: 0.06, 0.17), being of Chinese ethnicity (HR: 1.46; 95%CI: 1.04, 2.06), having a family history of pancreatic cancer (HR: 1.86; 95%CI: 1.13, 3.04), having hepatitis C (HR: 3.90; 95%CI: 1.69, 9.00), having hypertension (HR: 0.61; 95%CI: 0.42, 0.88), presenting with jaundice (HR 8.60; 95%CI: 4.95, 14.94), experiencing a lack of colour in faeces (HR: 3.15; 95%CI: 1.49, 6.64), having a palpable mass in the abdomen (HR: 2.35; 95%CI: 1.34, 4.13), the presence of ascites (HR: 2.52; 95%CI: 1.31, 4.86), haemoglobin (HR: 0.22; 95%CI: 0.16, 0.29), receiving palliative care (HR: 2.28; 95%CI: 1.39, 3.73), and end-of-life/ supportive care (HR: 6.47; 95%CI: 3.54, 11.85). All identified factors were associated with increased risk of mortality while being female, having hypertension, and higher haemoglobin values were linked with decreased mortality risk among pancreatic cancer patients. Table I presents the results of significant variables in univariable and

Table I: Prognostic factors on survival of pancreatic cancers after removing influential observations (n =357)

Variables	Simple Cox Proportional Hazard Regression		Multiple Cox Proportional Hazard Regression	
	Crude Hazard Ratio (95% CI)	p-value	Adjusted Hazard Ratio (95% CI)	p-value
Age group				
≤60 years old	1.00			
>60 years old	1.88 (1.37, 2.57)	<0.001		
Sex				
Male	1.00		1.00	
Female	0.78 (0.57, 1.06)	0.108	0.11 (0.06, 0.17)	<0.001
Ethnicity				
Malay	1.00		1.00	
Chinese	1.40 (1.02, 1.91)	0.037	1.46 (1.04, 2.06)	0.031
Indian	1.09 (0.63, 1.89)	0.747	0.84 (0.46, 1.56)	0.587
Marital status				
Single	1.00			
Married	2.01 (0.82, 4.94)	0.127		
Widow/Divorced	2.67 (1.05, 6.77)	0.038		
Smoking				
No	1.00			
Yes	1.48 (1.08, 2.02)	0.014		
Alcohol drinking				
No	1.00			
Yes	2.21 (1.18, 4.12)	0.013		
Family history of CA pancreas				
No	1.00		1.00	
Yes	1.39 (0.89, 2.18)	0.153	1.86 (1.13, 3.04)	0.014
Having pancreatitis				
No	1.00			
Yes	1.80 (0.91, 3.58)	0.093		
Having type II diabetes				
No	1.00			
Yes	1.79 (1.32, 2.42)	<0.001		
Having Hepatitis C				
No	1.00		1.00	
Yes	2.17 (1.01, 4.64)	0.047	3.90 (1.69, 9.00)	0.001
Having cirrhosis				
No	1.00			
Yes	5.29 (1.28, 21.86)	0.021		
Hypertension				
No	1.00		1.00	
Yes	1.36 (0.99, 1.87)	0.054	0.61 (0.42, 0.88)	0.009
Ischaemic Heart Disease				
No	1.00			
Yes	1.84 (1.06, 3.21)	0.031		
Abdominal pain				
No	1.00			
Yes	1.59 (1.18, 2.14)	0.002		
Back pain				
No	1.00			
Yes	1.76 (1.20, 2.58)	0.004		
Loss of appetite				
No	1.00			
Yes	2.17 (1.61, 2.93)	<0.001		
Fatigue				
No	1.00			
Yes	1.65 (1.20, 2.26)	0.002		
Nausea and vomiting				
No	1.00			
Yes	1.35 (0.99, 1.82)	0.056		
Jaundice				
No	1.00		1.00	
Yes	8.27 (5.67, 12.06)	<0.001	8.60 (4.95, 14.94)	<0.001
Lack of colour in faeces				
No	1.00		1.00	
Yes	7.07 (4.31, 11.60)	<0.001	3.15 (1.49, 6.64)	0.003

Table I: Prognostic factors on survival of pancreatic cancers after removing influential observations (n =357)

Variables	Simple Cox Proportional Hazard Regression		Multiple Cox Proportional Hazard Regression	
	Crude Hazard Ratio (95% CI)	p-value	Adjusted Hazard Ratio (95% CI)	p-value
Dark colour urine				
No	1.00			
Yes	5.67 (3.09, 10.43)	<0.001		
Fever				
No	1.00			
Yes	3.75 (2.57, 5.49)	<0.001		
Abdominal distension				
No	1.00			
Yes	2.12 (1.40, 3.19)	<0.001		
Dyspepsia				
No	1.00			
Yes	2.12 (1.46, 3.10)	<0.001		
Mass in abdomen				
No	1.00		1.00	
Yes	4.35 (2.72, 6.94)	<0.001	2.35 (1.34, 4.13)	0.003
Having hepatomegaly				
No	1.00			
Yes	2.40 (1.67, 3.44)	<0.001		
Having ascites				
No	1.00		1.00	
Yes	6.74 (4.10, 11.09)	<0.001	2.52 (1.31, 4.86)	0.006
Haemoglobin	0.40 (0.34, 0.47)	<0.001	0.22 (0.16, 0.29)	<0.001
Type of carcinoma				
Exocrine tumour	1.00			
Neuroendocrine tumour	0.39 (0.19, 0.80)	0.010		
Location of tumour				
Head	1.00			
Body	1.34 (0.84, 2.13)	0.221		
Tail	0.80 (0.47, 1.34)	0.395		
Treatment modality				
Surgery& adjuvant therapy	1.00		1.00	
Palliative care	1.92 (1.25, 2.95)	0.003	2.28 (1.39, 3.73)	0.001
End-of-life care	14.82 (9.12, 24.10)	<0.001	6.47 (3.54, 11.85)	<0.001

HR: Hazard ratio; CI: Confidence interval; Forward stepwise variable selection method was applied. Checking the linearity of the continuous variable, multicollinearity and two-way interaction terms, and no problem was identified. The preliminary final model was properly specified (_hat: P<0.037) (_hatsq: P=0.679). The Cox model assumptions were checked graphically by employing various diagnostic plots including the Hazard function plot, Log-minus-log plot, and Schoenfeld partial residuals plot. Additionally, the proportional hazard assumption was assessed for each individual variable in the preliminary final model using both the scaled Schoenfeld test (Separate test) and the unscaled Schoenfeld residual test (Global test) and the assumption was not violated. Regression diagnostics were performed by Martingale residuals, Cox-snell residuals, Deviance residuals and influential analysis. Remedial measures were applied, and two influential observations were omitted from the model.

multivariable analyses in terms of crude and adjusted hazard ratios (HR), their respective 95% CI values, and p-value.

DISCUSSION

Pancreatic cancer is a rapidly lethal malignant neoplasm with poor prognosis, characterized by the mortality to incidence ratio as high as 98%.[10] Given the severity of this disease, there is an urgent need for ongoing research efforts aimed at alleviating suffering and improving survival rates. With regards to this issue, the present study focused on 376 pancreatic cancer patients treated at State Hospitals in Malaysia, examined the multifaceted nature of its prognosis.

Globally, pancreatic cancer exhibits a slight male predominance in both the occurrence of new cases and mortality rates.[4] Consistent with these trends and previous local studies in Malaysia,[11-12] our study documented that nearly 60% of diagnosed cases were male, and female patients had 89% decreased risk of mortality compared to men. The effect of gender on survival outcomes is conflicting; some studies reported poorer survival outcomes among males,[13] while others found no significant gender impact.[14] The influence of gender on cancer survival is likely multifaceted, encompassing factors such as sex differences in molecular or genetic predisposition,[14] and variations in risk exposure, sex hormones, treatment allocation and treatment responses.[15] Furthermore, research exploring these aspects could provide deeper insights into how these factors influencing on gender disparity on pancreatic cancer survival.

Concerning ethnicity, Chinese individuals have historically shown higher rates of pancreatic cancer compared to other ethnicities in Malaysia.[16] However, in the present study, Malays constituted the majority of diagnosed patients, with

Chinese patients representing only 33.2% of the total patient population. This observed ethnic distribution discrepancy may stem from the fact that the majority of data for this study were obtained from State Hospitals which typically serve regions with a higher Malay resident population. In terms of survival outcomes, this study documented a higher mortality risk among Chinese patients compared to Malay cases. Racial disparities in pancreatic cancer incidence and survival may result from modifiable factors such as lifestyle, diet, and physical activity.[17] Genetic and molecular differences unique to each ethnic group could also affect the survival outcomes.[18] Furthermore, variations in cancer awareness and accessibility to healthcare among ethnic groups may contribute to these disparities.[19] However, this study lacked detailed data on these factors, highlighting the need for further research to identify the underlying mechanisms driving these disparities.

There is increasing evidence suggesting an association between a family history of pancreatic cancer and an elevated risk for non-affected family members to develop the disease.[20] In this study, 9.8% of the patients reported the family history, and they exhibited an 86% higher risk of mortality compared to those without such history. These findings are consistent with prior research by Ji et al. in 2008,[21] which also highlighted poorer survival in familial pancreatic cancer cases compared to sporadic cases. Conversely, a study by Omer, Boucher, and DiSario in 2004[22] observed that individuals with a family history of the disease exhibited longer survival, even after accounting for birth year and age at diagnosis. The existing literature on the impact of family history on the survival of pancreatic cancer cases remains limited and inconclusive. Nevertheless, it remains imperative to identify and conduct pancreatic cancer screening among familial high-risk individuals for early detection and timely treatment to promote longer survival.

Hepatitis B and hepatitis C viral infections are primarily linked to liver diseases. However, recent evidence suggests their potential association with extrahepatic malignancies, such as pancreatic cancer. A meta-analysis of observational studies done by Xu et al. in 2013[23] and a meta-analysis of cohort studies by Zhao et al. in 2023[24] provided compelling evidence that an increased risk of pancreatic cancer development with chronic infection of these viruses. In this current study, 2.9% and 2.1% of the total patients had hepatitis B and hepatitis C infection, respectively. Moreover, the study findings suggested that hepatitis C infection, rather than hepatitis B, was associated with a higher risk of mortality. Despite hepatitis B being more infectious than hepatitis C,[25] the latter lacks a vaccine and is more prone to becoming a chronic condition.[26] Their interplay with pancreatic cancer prognosis remains unclear, and understanding their relationship could offer valuable insights into the management and treatment of this malignancy.

Among patients with pancreatic cancer, hypertension is a frequently observed comorbidity, as evidenced by a retrospective study conducted in Poland revealing that 52.6% of such patients presented with hypertension.[27] In this study, 31.1% of the total patients were either on anti-hypertensive medication or had documented hypertension in their medical records. Given its prevalence and potential impact of co-incidence of cancer survival, their association is an area of growing interest, and has inspired its own field of onco-hypertension.[28] Owing to a paucity of data, the literature on their association with survival outcomes remains inconclusive. Interestingly, in our study, hypertension was found to be inversely related with pancreatic cancer mortality which is consistent with findings of 25-year mortality surveillance study.[29] A recent large population-based study in 2022 further demonstrated that pancreatic cancer patients with hypertension who were treated with angiotensin II receptor blockers (ARBs) or angiotensin I-converting enzyme (ACE) inhibitors experienced significantly longer survival. These medications are believed to exert protective effects by modulating pathways involved in tumour growth and metastasis.[30] It is plausible that the hypertensive patients in our study were more likely to be on these medications, which may have contributed to the observed inverse association between hypertension and mortality. However, our study lacked specific data on antihypertensive therapy, limiting our ability to confirm this hypothesis. This underscores the critical need for future research to explore the role of antihypertensive medications in pancreatic cancer survival.

Anaemia is a common occurrence in cancer patients. It affects around half of those undergoing systemic treatment and one-third prior to therapy initiation,[31] with pancreatic ductal adenocarcinoma (PDAC) patients being particularly susceptible.[32] The current study underscores the significance of haemoglobin levels as a crucial prognostic marker for pancreatic cancer patient survival, with lower values indicating an elevated risk of mortality. The literature suggested that nutritional deficiencies and systemic inflammation may impede haemoglobin synthesis, particularly in patients with advanced disease stage.[33] Furthermore, compelling evidence indicates that low haemoglobin levels are associated with poor response to treatment, especially in those with late-stage disease.[34] As a result, those with low haemoglobin values may face higher mortality risk.

In its early stages, pancreatic cancer is clinically asymptomatic. By the time symptoms become apparent, the disease has locally advanced or spread to nearby organs, most commonly to the liver.[35] The clinical presentations documented in this study were nearly comparable to the other studies.[12] Additionally, a considerable portion of patients exhibited clinical indicators suggestive of liver or peritoneal cavity metastasis, including jaundice, pale-coloured stools, abdominal mass, and ascites. The presence of these manifestations indicates advanced-stage disease, and those with such complications may receive less aggressive treatment[36] and might have negative impact on a patient's quality of life.[37] Consequently, in this study, individual presenting signs and symptoms of metastasis were found to have worse prognosis compared to those without such manifestations.

Pancreatic cancer remains a challenging malignancy with limited treatment options, among which surgical resection remains the primary curative approach. Consistent with existing literature, our study demonstrated that patients

undergoing surgical resection with curative intent had the longest survival, whereas those receiving palliative therapy or best supportive care had the poorest outcomes. This aligns with the clinical expectation that patients referred for palliative or supportive care are typically those with advanced, inoperable disease and poor prognoses. These findings underscore the critical importance of early diagnosis and timely surgical intervention. Previous reports have similarly emphasized that surgical resection offers the only chance for cure, although only 15%–20% of cases are diagnosed at a stage where surgery is feasible.[38] However, our study lacked detailed data on the specifics of surgical procedures and the types of chemotherapy or radiotherapy administered, limiting the scope of further analysis. Future research should address these gaps to provide a more comprehensive understanding of treatment approaches and their effects on survival outcomes.

CONCLUSIONS

This retrospective review over an 8-year period provides valuable insights into the prognostic factors influencing the survival of patients with pancreatic cancer, particularly within the Malaysian context. By identifying specific clinical and demographic variables—such as ethnicity, familial history, co-infections, and comorbidities—this research underscores the complexity and multifaceted nature of pancreatic cancer prognosis. The significant association of factors like hepatitis C co-infection, jaundice, and end-of-life care with poorer survival outcomes emphasizes the need for targeted clinical interventions and tailored patient management strategies. Conversely, the identification of protective factors, such as female gender, hypertension, and higher haemoglobin levels, offers new perspectives that could guide future therapeutic approaches. Understanding these prognostic indicators can aid health personnels in more accurately assessing patient risk profiles, thereby facilitating earlier and more personalized interventions. Future research should build on these findings, exploring how these and other factors can be integrated into comprehensive care plans that address the specific needs of diverse patient populations.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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REFERENCES

1. World Cancer Research Fund (WCRFI). Pancreatic cancer statistics - WCRF International. 2022. [cited March 2022]. Available from: https://www.wcrf.org/cancer-trends/pancreatic-cancer-statistics/
2. Hu JX, Lin YY, Zhao CF, Chen WB, Liu QC, Li QW, et al. Pancreatic cancer: A review of epidemiology, trend, and risk factors. World J Gastroenterol 2021; 27(27): 4298.
3. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Facts and Figures 2021. CA Cancer J Clin 2021; 71(1): 7-33.
4. Ilic I and Ilic M. International patterns in incidence and mortality trends of pancreatic cancer in the last three decades: A joinpoint regression analysis. World J Gastroenterol 2022; 28(32): 4698-715.
5. Halabi S and Owzar K. The importance of identifying and validating prognostic factors in oncology. Semin Oncol 2010; 37(2): e9-18.
6. World Health Organization (WHO). Malaysia (Source: Globocan 2018). 2019. [cited July 2020]. Available from: https://gco.iarc.fr/today/data/factsheets/populations/458-malaysia-fact-sheets.pdf
7. World Health Organization (WHO). Malaysia (Source: Globocan 2020). 2021. [cited February 2021]. Available from: https://gco.iarc.fr/today/data/factsheets/populations/458-malaysia-fact-sheets.pdf
8. Aung MMT, Naing NN, Hassan MRA, Wan-Arfah N, Chan H, Oo SS, et al. The median survival time of pancreatic cancer patients in Malaysia. Malaysian J Public Heal Med 2022; 22(3): 355-64.
9. StataCorp. Stata Statistical Software: Release 17. Published online 2021.
10. Capasso M, Franceschi M, Rodriguez-Castro KI, Crafa P, Cambiè G, Miraglia C, et al. Epidemiology and risk factors of pancreatic cancer. Acta Biomed 2018; 89(Suppl 9): 141-6.
11. Malwinder S, Wi WZ, Cimmeran K, Vce P, Austin TM. Prognostic factors for survival in pancreatic cancer patients from University Malaya Medical Centre, Malaysia. J Heal Transl Med 2018; 21(1): 6-13.
12. Norsa'adah B, Nur-Zafira A, Knight A. Pancreatic cancer in Universiti Sains Malaysia Hospital: a retrospective review of years 2001-2008. Asian Pacific J Cancer Prev 2012; 13(6): 2857-60.
13. Pijnappel EN, Schuurman M, Wagner AD, de Vos-Geelen J, Geest LGM vanDer, de Groot JWB, et al. Sex, gender and age differences in treatment allocation and survival of patients with metastatic pancreatic cancer: a nationwide study. Front Oncol 2022; 12: 1-9.
14. Önal Ö, Yılmaz SD, Eroğlu HN, Eroğlu İ, Koçer M. Survival analysis and factors affecting survival in patients with pancreatic cancer. Med Sci Discov 2020; 7(2): 412-18.
15. Radkiewicz C, Johansson ALV, Dickman PW, Lambe M, Edgren G. Sex differences in cancer risk and survival: a swedish cohort study. Eur J Cancer 2017; 84: 130-40.
16. Ministry of Health Malaysia. Press Release: Malaysia National Cancer Registry Report (MNCR) 2012-2016; 2019. [cited May 2021]. Available from: https://drive.google.com/file/d/1BuPWrb05N2Jez6sEP8VM5r6JtJtlPN5W/view
17. Rawla P, Sunkara T, Gaduputi V. Epidemiology of Pancreatic Cancer: Global Trends, Etiology and Risk Factors. Rev World J Oncol 2019; 10(1): 10-27.
18. Yamaguchi K, Chijiiwa K, Torato N, Kinoshita RTM, Tanaka M. Ki-ras codon 12 point and P53 mutations: a molecular examination of the main tumor, liver, portal vein, peripheral arterial blood and para-aortic lymph node in pancreatic cancer. Am J Gastroenterol 2000; 95(8): 1939-45.
19. Khalaf N, Xu A, Wenker TN, Kramer JR, Liu Y, Singh H, et al. The impact of race on pancreatic cancer treatment and survival in the nationwide veterans affairs healthcare system. Pancreas 2024; 53(1): e27–33.
20. Porter N, Laheru D, Lau B, He J, Zheng L, Narang A, et al. Risk of pancreatic cancer in the long-term prospective follow-up of familial pancreatic cancer kindreds. J Natl Cancer Inst 2022; 114(12): 1681-88.
21. Ji J, Försti A, Sundquist J, Lenner P, Hemminki K. Survival in familial pancreatic cancer. Pancreatology 2008; 8(3): 252-6.
22. Omer N, Boucher K, DiSario J. Survival outcomes in familial pancreatic cancer. Pancreas 2004; 29(4): 348.

23. Xu JH, Fu JJ, Wang XL, Zhu JY, Ye XH, Chen SD, et al. Hepatitis B or C viral infection and risk of pancreatic cancer: A meta-analysis of observational studies. World J Gastroenterol 2013; 19(26): 4234-41.
24. Zhao JF, Teng QP, Lv Y, Li XY, Ding Y. Association between hepatitis B or hepatitis C virus infection and risk of pancreatic cancer: a systematic review and meta-analysis of cohort studies. Ther Adv Infect Dis 2023; 10: 1-4.
25. Hepatitis B Foundation. What's the difference: hepatitis B vs hepatitis C? 2019. [cited April 2019]. Available from: https://www.hepb.org/blog/whats-the-difference-hepatitis-b-vs-hepatitis-c/
26. MedicalNewsToday (MNT). What is the difference between hepatitis B and C. 2023. [cited April 2023]. Available from: https://www.medicalnewstoday.com/articles/323455
27. Fudalej M, Cichowska I, Badowska-kozakiewicz A, Deptała A. The prevalence and impact of overweight and hypertension among patients with pancreatic cancer. Oncol Clin Pract 2024: 1-13.
28. Gudsoorkar P, Ruf R, Adnani H, Safdar K, Sparks MA. Onco-hypertension: an emerging specialty. Adv Chronic Kidney Dis 2021; 28(5): 477-89.
29. Batty GD, Shipley MJ, Marmot MG, Davey Smith G. Blood pressure and site-specific cancer mortality: Evidence from the original Whitehall study. Br J Cancer 2003; 89(7): 1243-7.
30. Keith SW, Maio V, Arafat HA, Alcusky M, Karagiannis T, Rabinowitz C, et al. Angiotensin blockade therapy and survival in pancreatic cancer: a population study. BMC Cancer 2022; 22(1): 1-9.
31. Ludwig H, Müldür E, Endler G, Hübl W. Prevalence of iron deficiency across different tumors and its association with poor performance status, disease status and anemia. Ann Oncol 2013; 24(7): 1886-92.
32. Osmola M, Gierej B, Mleczko-Sanecka K, Jończy A, Ciepiela O, Kraj L, et al. Anemia, iron deficiency, and iron regulators in pancreatic ductal adenocarcinoma patients: a comprehensive analysis. Curr Oncol 2023; 30(8): 7722-39.
33. Xu SS, Li S, Xu HX, Li H, Wu CT, Wang WQ, et al. Haemoglobin, albumin, lymphocyte and platelet predicts postoperative survival in pancreatic cancer. World J Gastroenterol 2020; 26(8): 828.
34. McGrane JM, Humes DJ, Acheson AG, Minear F, Wheeler JMD, Walter CJ. Significance of anemia in outcomes after neoadjuvant chemoradiotherapy for locally advanced rectal cancer. Clin Colorectal Cancer 2017; 16(4): 381-5.
35. Liu Z, Gou A, Wu X. Liver metastasis of pancreatic cancer: the new choice at the crossroads. Hepatobiliary Surg Nutr 2023; 12(1): 88-91.
36. Han MY and Borazanci EH. Malignant ascites in pancreatic cancer: Pathophysiology, diagnosis, molecular characterization, and therapeutic strategies. Front Oncol 2023; 13.
37. Czerw A, Partyka O, Pajewska M, Badowska-kozakiewicz A, Fudalej M, Sygit K, et al. Quality of life in patients with pancreatic cancer — a literature review. Int J Env Res Public Heal 2023; 20(6): 1-11.
38. De La Cruz MSD, Young AP, Ruffin MT. Diagnosis and management of pancreatic cancer. Am Fam Physician 2014; 89(8): 626-32.