

Cancer Diagnosis in Hypertensive Heart Disease Population: A Cross Sectional Study in Soetomo General Hospital

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SOUHRN

Hypertenze jako globální zdravotnický problém stále není dostatečně léčena; výsledkem jsou změny ve struktuře a funkci srdce, které jsou spojeny s hypertenzní nemocí srdce (hypertensive heart disease, HHD). Přitom se při nádorovém onemocnění s charakteristickou abnormální proliferací buněk začínají buňky chovat jinak a jinak odpovídat na léčebné strategie. Přes značné úsilí zůstávají některé druhy nádorů nevyléčitelné, což znamená, že kardiovaskulární onemocnění a nádorové onemocnění představují celosvětově hlavní příčiny úmrtí na nepřenosná onemocnění. Ve snaze získat další informace o této shodě jsme provedli průřezovou studii incidence nádorových onemocnění u pacientů s HHD léčených ve všeobecné nemocnici dr. Soetoma. Průměrný věk hodnocené populace byl 58,1 roku a průměrná hodnota BMI 25,9. Nalezli jsme statisticky významnou spojitost mezi pohlavím a dobou od stanovení diagnózy hypertenze na jedné straně a přítomností nádorového onemocnění u populace s HHD na straně druhé. Získané údaje konkrétně ukazují, že u žen s HHD existuje vyšší pravděpodobnost vzniku některých typů karcinomů, zvláště prsu a gynekologických. Další typy nádorů byly nalezeny v prostatě, krvi a v lymfatickém systému, hlavě a krku, v plicích, štítné žláze a v ledvinách. Analýza nicméně neprokázala spojitost mezi dobou od stanovení diagnózy hypertenze a prevalencí nádorového onemocnění. Za zmínku stojí zvláště zjištění starších studií, že korelace mezi nádorovým onemocněním a hypertenzí nesouvisí s užíváním antihypertenziv, protože stejné riziko lze pozorovat i u neléčených pacientů. Několik rizikových faktorů společných pro hypertenzi a nádorové onemocnění ukazuje na překryv základních molekulárních patofyziologických mechanismů obou onemocnění. Budoucí, lépe navržené studie se musejí zaměřit na další společné faktory hypertenze a nádorových onemocnění u větších souborů pacientů.

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ABSTRACT

Hypertension as a global concern remains inadequately controlled, ultimately leading to cardiac structural and functional changes associated with hypertensive heart disease (HHD). Simultaneously, cancer, characterized with abnormal cell proliferation, exhibits diverse behaviours and responses to treatment strategies. Despite extensive efforts, certain type of cancers remains incurable, making both cardiovascular diseases and cancer the leading causes of non-communicable disease mortality in the world. To investigate this association, we conducted a cross-sectional study, reporting the incidence of cancer in the HHD population at Soetomo General Hospital. The population is characterized by a mean age of 58.1 years and a mean BMI of 25.9. We found a significant association between sex and the duration of hypertension and the presence of cancer in the HHD population. Specifically, the data indicate that females with HHD have a higher likelihood of having certain cancer types particularly breast and gynaecologic cancers. Additional types of cancer included prostate, blood & lymphatic system, head & neck, lung, thyroid, and renal cancers. Unfortunately, the analysis failed to demonstrate the association between duration of hypertension and the presence of cancer. Notably, previous studies revealed that the correlation between cancer and hypertension is not linked to the administration of antihypertensive medications, as the risk is also observed in untreated patients. Several shared risk factors between hypertension and cancer imply the existence of overlap in molecular pathophysiological mechanisms underlying both conditions. Future studies shall be conducted to explore further regarding the association of hypertension and cancer incidence with larger population and better-designed research.

Keywords:

Cancer

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Introduction

Currently, the global prevalence of hypertension reaches 26.4% of the population, which accounts for 1.1 billion people. Unfortunately, only one in five people manages to adequately control their blood pressure. Prolonged hypertension eventually leads to cardiac structure and function changes that lead to heart failure.¹ Hypertensive heart disease (HHD) is a condition secondary to hypertension, that alters the cardiac structure and function.^{2,3} It was caused by the chronic elevation of blood pressure. In order to compensate for pressure overload, the main feature of HHD is left ventricular hypertrophy (LVH). The pathophysiology of HHD involved abnormal growth of cardiomyocytes, increased collagen production, and mechanical stress-induced neurohormonal agent production.⁴ Whereas cancer is an abnormal proliferation of any kind of cell in the body, it can be diverse in its behaviour and response to treatment strategies.⁵ Solid cancerous growth often develops from epithelial lining cells of various organs, including gastrointestinal tract, genitourinary tract, and the reproductive tract. Although there have been extensive medical and public health initiatives to develop numerous treatment strategies, the majority cancers still remain incurable and result in the premature death of millions of people annually.⁶

Unfortunately, both cardiovascular diseases and cancer are the leading mortality causes of non-communicable disease in the world.⁷ As the occurrence of both conditions continues to rise, there is an expanding demographic that is at risk of experiencing these conditions simultaneously.⁸ This condition may be confounded by similar risk factors such as age, physical inactivity, metabolic syndrome, tobacco use, alcohol consumption or just merely closer medical surveillance. In 1975, Dyer et al. initiated a prospective study to explore the potential association between hypertension and cancer, and this connection has since been a subject of ongoing discussion, with numerous cohort studies consistently reaffirming similar findings.^{9,10} Potential mechanisms include increased production of inositol triphosphate and increased levels of cytosolic calcium.¹¹ Two main hypotheses have been proposed to clarify this connection. First, antihypertensive medications were initially suspected of contributing to cancer by promoting carcinogenesis, enhancing other cancer-inducing factors, or hindering the body's defence mechanism. Alternatively, blood pressure regulation is also assumed to be related to cancer development, irrespective of hypertension treatment. It is also plausible that cancer itself could lead to hypertension.¹² Therefore, we aim to explore the association between hypertension and cancer through conducting a cross-sectional study to report the incidence of cancer at the HHD population in Soetomo General Hospital.

Methods

Research design

This retrospective cross-sectional study used secondary data from the medical records in the outpatient unit of Soetomo General Hospital, Surabaya, Indonesia. We par-

ticularly used outpatients in the Department of Cardiology and Vascular Medicine. This study included all patients who were diagnosed with hypertensive heart disease (HHD) based on ICD 10. Then, we traced the collected data based on their visit to the outpatient unit. Thus, this study collected 90 samples.

From the medical records, we gathered several data including age, sex, body mean index (BMI), duration of hypertension, blood pressure, comorbidity factors, and a type of cancer. Comorbidity factors include coronary artery disease (CAD), diabetes mellitus, peripheral artery disease (PAD), stroke, and chronic kidney disease (CKD). We also sorted out the comorbidity factors with the ICD 10 diagnosis code. The subjectivity of writing the medical records would not affect our data since it did not involve any physical examinations or input from the attending physician. Therefore, all the data utilized in this research is considered reliable. In terms of validity, this study also deliberately left out incomplete medical records.

Data analysis

Statistical analysis was performed to determine the association between cancer and HHD, with IBM SPSS Statistics 26.0. The statistical significance level was set at 0.05. Continuous variables, presented as mean \pm SD, were evaluated for normal distribution and compared using the chi square test, as appropriate.

Results

After gathering samples, we summarize the patients' characteristics in **Table 1**. We found that the mean age of our samples is 58.1 years. 57.1% of the samples that were included are female ($n = 52$). The mean BMI of our samples is 25.9 which can be categorized as overweight. Moreover, we categorized the duration of hypertension into <5 years and ≥ 5 years. Most patients were diagnosed with hypertension for less than 5 years ($n = 61$; 67.0%). The mean systolic and diastolic blood pressure of our samples are 141.5 and 81.2 mmHg, respectively. These values are categorized above the normal value.

The comorbidity factors of our samples showed that most patients had CAD and diabetes mellitus ($n = 30$; 33.0%), that was followed by stroke ($n = 6$; 6.6%), CKD ($n = 4$; 4.4%), and PAD ($n = 3$; 3.3%). We also classify the cancer based on the affected organ. Our samples showed that most patients had breast and gynaecologic cancer ($n = 10$; 28.6%), followed by prostate ($n = 5$; 14.3%), blood & lymphatic system ($n = 5$; 14.3%), head & neck ($n = 2$; 5.7%), lung ($n = 1$; 2.9%); thyroid ($n = 1$; 2.9%); and renal ($n = 1$; 2.9%).

We analyze the association between sex and duration of hypertension and the presence of cancer in the HHD population. The chi-square analysis suggests that there is a statistically significant association between sex and the presence of cancer in our sample, the HHD population. Specifically, the data indicate that females with HHD have a higher likelihood of having cancer compared to their male counterparts.

Table 1 – Baseline characteristics

No.	Description	n (%) or mean \pm SD
1	Age (Years)	58.1 \pm 12.0
2	Sex	
	Male	38 (41.8%)
	Female	52 (57.1%)
3	BMI	25.9 \pm 5.2
4	Duration of hypertension	
	<5 years	61 (67.0%)
	\geq 5 years	29 (31.9%)
5	Systolic blood pressure	141.5 \pm 23.2
6	Diastolic blood pressure	81.2 \pm 15.2
	Heart failure sign & symptoms	
7	Comorbidity factors	
	Coronary artery disease (CAD)	30 (33.0%)
	Diabetes mellitus	30 (33.0%)
	Stroke	6 (6.6%)
	Chronic kidney disease (CKD)	4 (4.4%)
	Peripheral artery disease (PAD)	3 (3.3%)
8	Classification of cancer	
	Breast	10 (28.6%)
	Gynaecologic	10 (28.6%)
	Prostate	5 (14.3%)
	Blood and lymphatic system	5 (14.3%)
	Head and neck	2 (5.7%)
	Lung	1 (2.9%)
	Thyroid	1 (2.9%)
	Renal	1 (2.9%)

Unfortunately, the chi-square analysis failed to demonstrate the association between duration of hypertension and the presence of cancer in HDD population. Details regarding analyzed data are presented in **Tables 2 and 3**.

Discussion

In this study, we included a population with a mean age of 58.1 years, with a majority of 57.1% being female (n = 52). The mean BMI of the population is 25.9. The most prevalent comorbidities are CAD and diabetes mellitus, affecting 33.0% of the population (n = 30). Statistical analysis revealed a significant association between sex and the prevalence of cancer in the hypertensive population. Unfortunately, no statistically significant association was observed between the duration of hypertension and cancer prevalence.

Coincidence of cancer and hypertension

Previous research has established a bidirectional relationship between hypertension and cancer.¹³ The relationship between hypertension and cancer was first discovered in a prospective study in 1975 by Dyer et al. There exists

Table 2 – Sex and cancer

Cancer	Sex		p-value
	Male	Female	
(–)	31 (34.4%)	24 (26.7%)	0.000662*
(+)	7 (7.8%)	28 (31.1%)	
Total	38 (42.2%)	52 (57.8%)	

*p < 0.05 significantly

Table 3 – Duration of hypertension and cancer

Duration of hypertension	Without cancer	With cancer	p-value
<5 years	36	25	0.554382
\geq 5 years	19	10	
Total	55	35	

a positive correlation between the presence of cancer and the likelihood of developing hypertension.¹⁴ Hypertension has been linked to an elevated risk of developing certain types of cancer, with a higher cancer-related mortality.¹⁰ Hence indicating that the association between these two phenomena is not merely coincidence.¹⁴

Cancer and hypertension shared risk factors

Various mechanisms could potentially elaborate on the association between hypertension and cancer. It is important to note that hypertension and cancer share similar risk factors. Several hypertensive risk factors, such as advanced age, smoking, obesity, and a sedentary lifestyle, have been identified as contributors to the development of cancer incidence, mortality, and morbidity.^{10,15–17} Additionally, obesity has been identified as a notable predictor of endometrial, renal, and liver cancer in women.⁹ Moreover, it has been found that anticancer medications have the potential to elevate blood pressure levels.¹⁶ Nevertheless, it is important to note that antihypertensive therapy does not appear to be associated with an increased risk of cancer development. It is supported by the similar risk levels between hypertensive individuals who are treated and untreated.¹² However, other studies have observed statistically that antihypertensive therapy is a predictor of the development of kidney and pancreatic cancer in women, whereas no such association has been found in males.⁹

Several shared risk factors between hypertension and cancer imply the existence of overlap in molecular pathophysiological mechanisms underlying both conditions. Chronic inflammation is suggested to be potential basis for both diseases, given its association with underlying risk factors such as obesity, diabetes mellitus, smoking, and others.¹⁸ Oxidative stress also appears to be the pathogenesis associated with hypertension and cancer.¹³ The exact mechanisms have not been clear. Animal model studies have demonstrated that there appears to be dysregulation of apoptosis linked to hypertension. Furthermore, hypertensive individuals also showed elevated levels of angiotensin II, leading to the stimulation of

vascular endothelial growth factor (VEGF) production, which consequently initiates the angiogenesis process in patients with cancer.¹⁸

Cancer classification in hypertensive population

There are certain types of cancers that are suggested to be related to hypertension. The North Korean hypertension registry documented a higher incidence of kidney, pancreatic, and endometrial cancer among hypertensive patients. Conversely, there has been a decline in the prevalence of lung cancer.⁹ A meta-analysis also identified a significant link between hypertension and renal, colorectal, and breast cancer.¹⁹ In this study, the most prevalent types of cancer are breast and gynaecologic cancers, that are accountable for 28.6% of the population (n = 10). Other type of cancers that were found in this study are prostate cancer, blood & lymphatic system cancer, head & neck cancer, lung cancer, thyroid cancer, and renal cancer.

In terms of sex comparison, multiple research projects have identified a positive correlation between hypertension and cancer among male patients. However, certain studies have also demonstrated a similar association among female patients.^{10,20} The presence of hypertension in males has been found to be correlated with an increasing susceptibility to prostate cancer, whereas hypertension in females has been linked to an elevated risk of developing endometrial and breast cancer.²¹ However, the association between hypertension and prostate cancer remains considerably debatable. According to a registry study conducted in Sweden, there is evidence suggesting that hypertension may actually decrease the risk of developing prostate cancer. However, the underlying mechanism remains unclear.²⁰ Nevertheless, previous studies revealed a significant elevation in the likelihood of developing prostate cancer among individuals diagnosed with hypertension.²²

Among women, there is a well-known correlation between hypertension, along with other metabolic disorders, and the risk of developing breast cancer. The presence of hypertension is associated with an estimated increase in the risk of breast cancer, ranging from 14% to 23%. The correlation is not associated with the administration of antihypertensive medications, as the risk is also observed in non-treated patients.²³ In the context of urogenital cancer, a recent population-based study conducted in Taiwan has revealed a notable increase in the likelihood of uterine and kidney cancer occurrence among those with hypertension, as compared to normotensive patients. It also revealed that the aforementioned risk was more prominent among hypertensive individuals with a younger age and longer follow-up duration.²⁴

Strengths and limitation

The strengths of the present study are providing valuable descriptive data about the characteristics of the population with hypertension and cancer, including comorbidities and risk factors. There are also limitations to this work. Detection bias may play a crucial role because individuals with hypertension are under closer medical surveillance,

which leads to earlier detection of cancer compared to other untreated patients. Future studies shall be conducted to explore further regarding the association of hypertension and cancer incidence with larger population and better-designed research.

Conclusion

After conducting a cross-sectional study at Soetomo General Hospital, we found that the patients' characterized with mean age of 58.1 years and mean BMI of 25.9, which can be categorized as overweight. Moreover, the mean systolic and diastolic blood pressure of our samples is 141.5 and 81.2 mmHg, respectively. These values are categorized above the normal value. We found a significant association between sex and duration of hypertension and the presence of cancer in the HHD population. Specifically, the data indicate that females with HHD have a higher likelihood of having certain cancer types, particularly breast and gynaecologic cancers. Additional types of cancer included prostate, blood & lymphatic system, head & neck, lung, thyroid, and renal cancers.

Authors' contributions

We confirmed that we have contributed significantly to this study. All listed authors have reviewed and approved the final version of the manuscript, also agreed to the submission. Conceptualization & drafting, MA, WW, and ZZ; data collection and analysis ZZ, WW and HA; manuscript writing MA, WW, ZZ, HA; evaluation MA, WW, ZZ, and HA; supervision & editing MA and ZZ.

Conflict of interests

The authors declare no competing interests.

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We disclose any potential conflicts of interest, financial or otherwise, that might be perceived as influencing the content of this study.

Ethics approval and consent to participate

This research received an approval from Soetomo General Hospital. The research protocol was submitted to the committee, and all ethical considerations, potential risks, and protection of participants' rights were thoroughly evaluated.

Availability of data and material

We agree to make the relevant data and materials of the case report available to the journal and readers, upon reasonable request, to ensure transparency and reproducibility.

References

1. Moreno MU, González A, López B, et al. Hypertensive Heart Disease. *Encycl Cardiovasc Res Med* 2023;1–4:517–526.
2. Oparil S, Acelayado MC, Bakris GL, et al. Hypertension. *Nat Rev Dis Prim* 2018;4:18014.
3. Santos M, Shah AM. Alterations in cardiac structure and function in hypertension. *Curr Hypertens Rep* 2014;16:1–10.

4. Magyar K, Gal R, Riba A, et al. From hypertension to heart failure 2015;5:85–92.
5. Cooper GM. The Development and Causes of Cancer. Sunderland (MA): Sinauer Associates, 2000. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK9963/>
6. Harris RE. Global Epidemiology of Cancer. Google Books. 2021. Available from: https://books.google.co.id/books?hl=en&lr=&id=3lbUCQAAQBAJ&oi=fnd&pg=PR1&dq=worldwide+epidemiology+of+cancer&ots=1JsaK-7Wy&sig=TAB8HQugfRnVTFGm8TpAtlCf0hk&redir_esc=y#v=onepage&q=worldwide+epidemiology+of+cancer&f=false
7. ReFaey K, Tripathi S, Grewal SS, et al. Cancer Mortality Rates Increasing vs Cardiovascular Disease Mortality Decreasing in the World: Future Implications. Mayo Clin Proc Innov Qual Outcomes 2021;5:645.
8. Vincent L, Leedy D, Masri SC, Cheng RK. Cardiovascular Disease and Cancer: Is There Increasing Overlap? Curr Oncol Rep 2019;21:1–13.
9. Lindgren AM, Nissinen AM, Tuomilehto JO, Pukkala E. Cancer pattern among hypertensive patients in North Karelia, Finland. J Hum Hypertens 2005;19:373–379.
10. Mohammed T, Singh M, Tiu JG, Kim AS. Etiology and management of hypertension in patients with cancer. Cardio-Oncology 2021;7:1–13.
11. Grossman E, Messerli FH, Boyko V, Goldbourt U. Is there an association between hypertension and cancer mortality? Am J Med 2002;112:479–486.
12. Harding JL, Sooriyakumaran M, Anstey KJ, et al. Hypertension, antihypertensive treatment and cancer incidence and mortality: A pooled collaborative analysis of 12 Australian and New Zealand cohorts. J Hypertens 2016;34:149–155.
13. Cohen JB, Brown NJ, Brown SA, et al. Cancer Therapy-Related Hypertension: A Scientific Statement from the American Heart Association. Hypertension 2023;80:E46–E57.
14. Hamet P. Cancer and Hypertension. Hypertension 1996;28:321–324.
15. Warren GW, Alberg AJ, Kraft AS, Cummings KM. The 2014 Surgeon General's report: "The health consequences of smoking – 50 years of progress": a paradigm shift in cancer care. Cancer 2014;120:1914–1916.
16. Arem H, Moore SC, Patel A, et al. Leisure time physical activity and mortality: a detailed pooled analysis of the dose-response relationship. JAMA Intern Med 2015;175:959–967.
17. Arnold M, Pandeya N, Byrnes G, et al. Global burden of cancer attributable to high body-mass index in 2012: a population-based study. Lancet Oncol 2015;16:36–46.
18. Koene RJ, Prizment AE, Blaes A, Konety SH. Shared Risk Factors in Cardiovascular Disease and Cancer. Circulation 2016;133:1104–1114.
19. Seretis A, Cividini S, Markozannes G, et al. Association between blood pressure and risk of cancer development: a systematic review and meta-analysis of observational studies. Sci Reports 2019;9:1–12.
20. Stocks T, Van Hemelrijck M, Manjer J, et al. Blood pressure and risk of cancer incidence and mortality in the metabolic syndrome and cancer project. Hypertension 2012;59:802–810.
21. Tini G, Sarocchi M, Tocci G, et al. Arterial hypertension in cancer: The elephant in the room. Int J Cardiol 2019;281:133–139.
22. Liang Z, Xie B, Li J, et al. Hypertension and risk of prostate cancer: a systematic review and meta-analysis. Sci Reports 2016;6:1–7.
23. Peeters PHM, Van Noord PAH, Hoes AW, et al. Hypertension and breast cancer risk in a 19-year follow-up study (the DOM cohort). Diagnostic investigation into mammarian cancer. J Hypertens 2000;18:249–254.
24. Sun LM, Kuo HT, Jeng LB, et al. Hypertension and subsequent genitourinary and gynecologic cancers risk: A population-based cohort study. Medicine (Baltimore) 2015;94:e753.