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The Relationship Between Association Between Blood Pressure and Risk of Cancer

Development

Professor Nikolaos Tzenios Ph.D., FRSPH, FRSM, FAAMFM, FWAMS, FMRS, AcIASS, mRSB, DABAAHP¹, Dr. Mary E. TAZANIOS, MD ObGyn², and Mohamad Chahine, Ph.D.³

¹ Public Health and Medical Research, **Charisma University**, Grace Bay, Turks and Caicos Islands,

Train to Teach in Medicine, Department of Postgraduate Medical Education, Harvard Medical School, Boston, Massachusetts, USA,

Doctor of Health Sciences Candidate, **MCPHS University**, Boston, Massachusetts, USA

Harvard Medical School Postgraduate Medical Education High Impact Cancer Research 2019-2021

² Clinical Research, TRG GEN+, Beirut, Lebanon

³ Biological and Chemical Technology, International Medical Institute, Kursk State Medical University, Kursk, Russian Federation.

Corresponding Author:

Professor Nikolaos Tzenios Ph.D., FRSPH, FRSM, FAAMFM, FWAMS, FMRS, AcIASS, mRSB, DABAAHP¹ 3 Walham Yard, SW61JA, London, UK

Email address: Nicolas@Trccolleges.com

Abstract

Background of the Study

We investigated the link between hypertension and cancer since it has been suggested that hypertension may raise the long-term risk of cancer. Previous large observational cohort studies found that greater blood pressure (BP) was related to a higher risk of cancer. Mendelian randomization (MR) was utilized to produce less confounded blood pressure estimates (BP) on overall and site-specific malignancies. The study aims to draw conclusions on the relationship between high blood pressure and cancer.

Methods

Studies on high blood pressure and various malignancies are inconclusive, except for renal cell carcinoma. However, given that most meta-analyses only contained a limited number of trials, some relative risks had small to moderate magnitudes, and several may have been impacted by residual confounding, careful interpretation is necessary. The study was conducted using the meta-analysis technique. Cochran's Q test and I² test were used to assess statistical heterogeneity between studies in the current investigation for research involving two or more cause and outcome combinations.

Results

Positive correlations were also reported between high blood pressure and esophageal adenocarcinoma, squamous cell carcinoma, liver, and squamous cell carcinoma. However, most studies lacked multivariable adjustments. Physical and numerical risk of cardiovascular disease is linked to bowel cancer but no other cancers. According to a meta-analysis, hypertensive

persons could also be at increased danger of gastrointestinal and breast cancer. Most meta-analyses comprised several trials with moderate or mild hazard ratios.

Conclusion

Different types of cancers have been noted to be directly caused by hypertension. In addition, some treatments have also been associated with the side effects of cancer treatments to cause hypertension. Women facing hypertension have an increased risk of getting breast cancer. Although some cancers showed a real relationship with hypertension, others had no connection at all.

Keywords: high blood pressure, Cancer, malignancies, hypertension

Introduction

Both high blood pressure and cancer are serious, long-term diseases whose causes are complex. About one-third of all persons over 20 have hypertension, making it a primary cause of death and disability (Go et al., 2014). Men are more affected by high blood pressure compared to women (Centers for Disease Control and Prevention, 2022). Nearly half of all fatalities from cardiovascular causes, stroke, and cardiovascular disease in 2015 were attributable to high blood pressure (Forouzanfar et al., 2017). In addition, hypertension and its linked problems account for an estimated 10% of total healthcare costs (Campbell et al., 2014). According to World Health Organization (WHO) (2021), about 46% of mature people suffer from high blood pressure because they are unaware. About half of the cardiovascular ailments reported in the world hail from Asia (Soenarta et al., 2020). Hypertension is a lifestyle disease that increases women's risk of breast cancer (Lofterød et al., 2020).

Cancer was observed to be one of the diseases with the highest death rates (World Health Organization, 2022). About 18 million people were diagnosed with cancer in 2018, and 9.6 million people died from the disease. The number is even higher when hypertension is coupled with cancer (Stocks et al., 2012). These figures will likely climb over the next twenty years (Ferlay et al., 2019). If elevated and high blood pressure is linked to an increased risk of cancer, this could have significant implications for public health. In Karelia, Finland, it was observed that hypertension patients had a greater risk of developing kidney cancer (Tini et al., 2019). In pregnant women, hypertension also led to solid cancer cases (Behrens et al., 2016). Although renal cancer has long been associated with hypertension, no solid results prove the same (Sun et al., 2015). Uncertainty remains about hypertension's potential significance as a poor predictive factor for cancer-specific mortality (Petrelli et al., 2017).

Although it is unclear whether reverse causation accounts for all or part of the association between hypertension and renal cell carcinoma, the two conditions have been repeatedly linked. Cancers of the colon, breast, endometrium, and prostate have all been linked to glyphosate, but the data is weak (Aune et al., 2017). However, many recent studies have looked into the link between insulin resistance (in which hypertension figures prominently) and cancer risk. Therefore, we did a systematic evaluation and meta-analysis to examine the existing research (Esposito et al., 2014).

Methods

Using the accompanying search technique, we looked for suitable previous papers in PubMed from the beginning through November 2022. We carefully checked the cited works of relevant systematic and anecdotal reviews to ensure no studies were missed. Indicators of hypertension included a history of hypertension in the family, a measured systolic blood pressure (SBP) or diastolic blood pressure (DBP) that is higher than established cut-off thresholds (e.g., WHO guidelines), and treatment with medication for hypertension.

We employed the component for hypertension only when the sensitivity was endocrine disorder. Studies of pre-malignant outcomes, particular instance or instance, bridge studies, intense predictive studies among people with cancer, studies in young kids, study designs with a random sample of fewer than 100 people, literature reviews with less than 100 cases of cancer, studies that did not provide sufficient data for measuring associations, studies in languages other than English, and experiments with several respondents of less than 100 people were all excluded (e.g., colorectal adenomas). When published papers discussed the same cohort assessed over a range of follow-up times, we kept the report with the longer follow-up.

Each eligible study's author, publication year, journal, sample size, population details, description of high blood pressure, the likelihood of an event of arterial blood pressure (RR), 95% probability value of the cardiac index (CI), and adjustments for variables were noted. We always kept the most modified model when numerous statistical models' findings were provided. To evaluate the included studies' quality, we used the "Newcastle-Ottawa Scale." Each study was given points based on eight quality criteria categorized into three areas: I study selection; ii) binary compatibility of study groups; and iii) exposed or actual result elucidation for a particular circumstance and motley crew studies, respectively. For the best quality research, nine stars were given for all the quality items (Moskalewicz & Oremus, 2020)).

Previous studies have utilized the terms "cancer" and "hypertension." However, for this study, we only sought to include studies that showed hypertension and an increased risk of incident cancer. In order to find the data, a manual review was performed, which required five months. Databases like PubMed and Embase were utilized to look up papers published up through June 2021 to perform the literature review required for this investigation. The study's search criteria were as follows: (metabolic syndrome OR hypertension OR high blood pressure). Using this search procedure, it was possible to find all relevant studies examining the relationship between systolic and diastolic blood pressures and organ-specific cancer locations using clinical cohorts and case-controlled studies (Seo et al., 2020). The search for viable articles and publications was done through www.google.com and also from www.ncbi.nlm.nih.gov.

Even if the research was supposed to be about metabolic syndrome, a cluster of conditions including obesity, high triglyceride levels, and high blood pressure, just the hypertension information was analyzed and collected (Tzenios et al., 2022). Measurements, medical histories, and questionnaires were used to collect data, and high blood pressure was

defined as a reading that was consistently greater than the study's baseline. The studies were evaluated using the following standards: (1) Case-control studies were required; (2) they had to report an absolute risk, incidence rate, or coefficient of determination that could be transformed into an absolute risk; (3) the publicity was high blood pressure, and the result was unexpected cancer risk.

Data Extraction

Reviewers examine the investigation's description before beginning the manual data extraction process. There was no coordination between the extraction of author information, study location, publication date, study methodology, and the hypertension definition: thirty cohort studies, sixteen case-control studies, and one mystery study made up the total.

Statistical Analysis

Depending on the type of analysis performed, statistical software produced possible costs or an odds ratio based on data from previous research on the individual cases. Significance levels and summarized relative risks with 95% certainty were determined in the primary analysis. The odds ratios from a handful of the included studies were transformed into possible costs (Grant, 2014). Additionally, studied were hypertension and dose-dependent systolic and diastolic blood pressure per 10 mmHg (Stare & Maucort-Boulch, 2016)). Cochran's Q test and I2 test were used to assess statistical heterogeneity between studies in the current investigation for research involving two or more cause and outcome combinations (Jafari & Ansari-Pour, 2019). For the statistical work, we used Excel Spreadsheet (Deeks et al., 2019).

Study characteristics

As shown in Figure 1, the meta-analysis includes only studies that meet specific criteria. In the beginning, 73,652 references were verified after keyword searches were performed on databases. Throughout the whole screening process, no automation technology was used. Before November 2022, 55 studies were uncovered by a manual search of the relevant literature. The primary inclusion criteria were studies published after 2017 showing a positive connection between high blood pressure and an elevated risk of incidental cancer.

There were originally 80 papers that were screened; however, we had to eliminate 17 due to their focus on pathology, mortality, a previous meta-analysis/review, a lack of hypertension information, and the inclusion of antihypertensive medicines, as well as five that were duplicates ($n = 75$). Twenty-five studies were selected using this strategy. Given that the 148 studies in the last meta-analysis ended in 2017, we did a new hand search to isolate the 66 studies that will fall between 2017 and June 2021.1 (Seretis et al., 2019). After completing a manual search for research from 2017-2021, 22 were located. A total of 47 studies were located without the aid of cognitive computing.

Figure 1

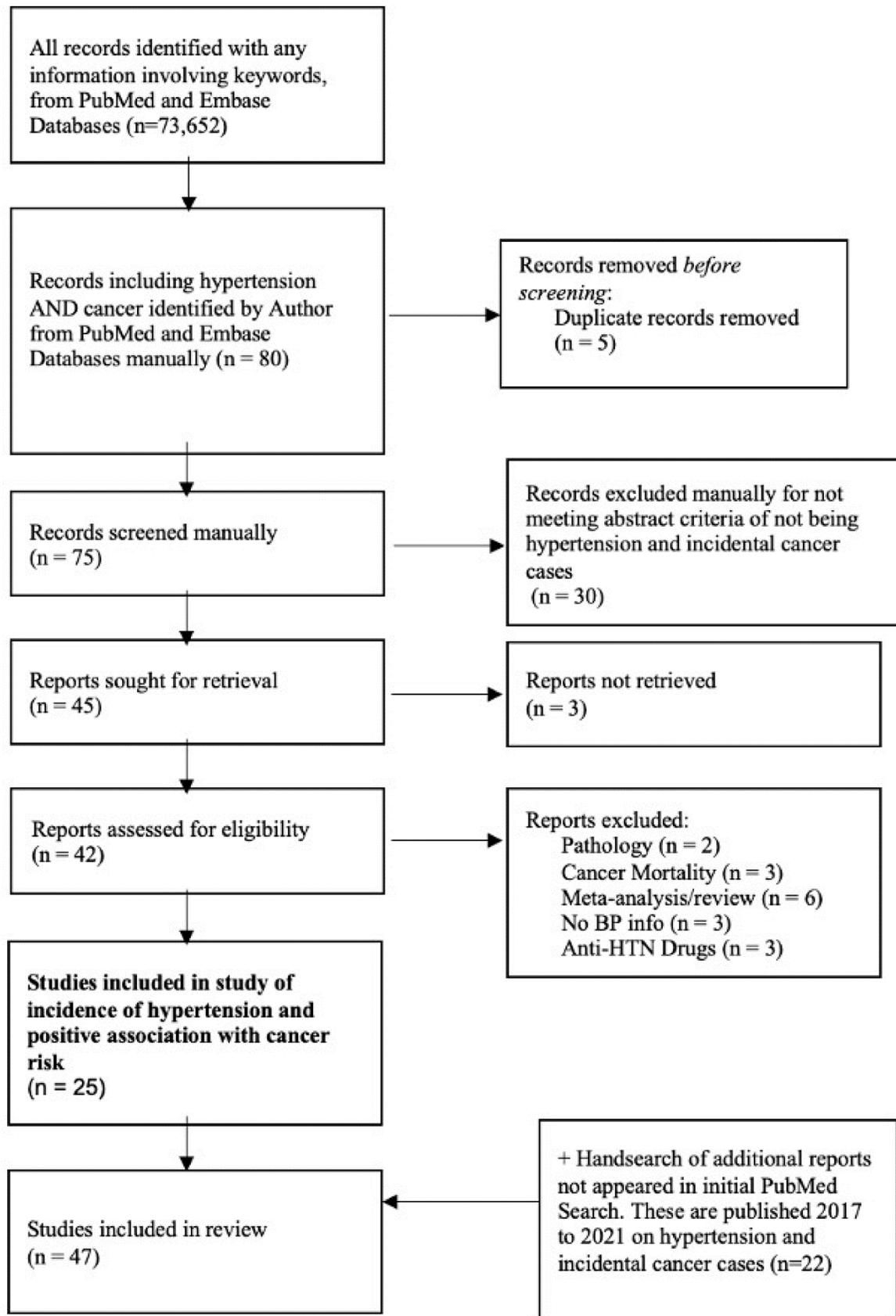


Figure 1 derived from <https://www.nature.com/articles/s41598-019-45014-4/figures/1>

Evidence synthesis

Tables 1

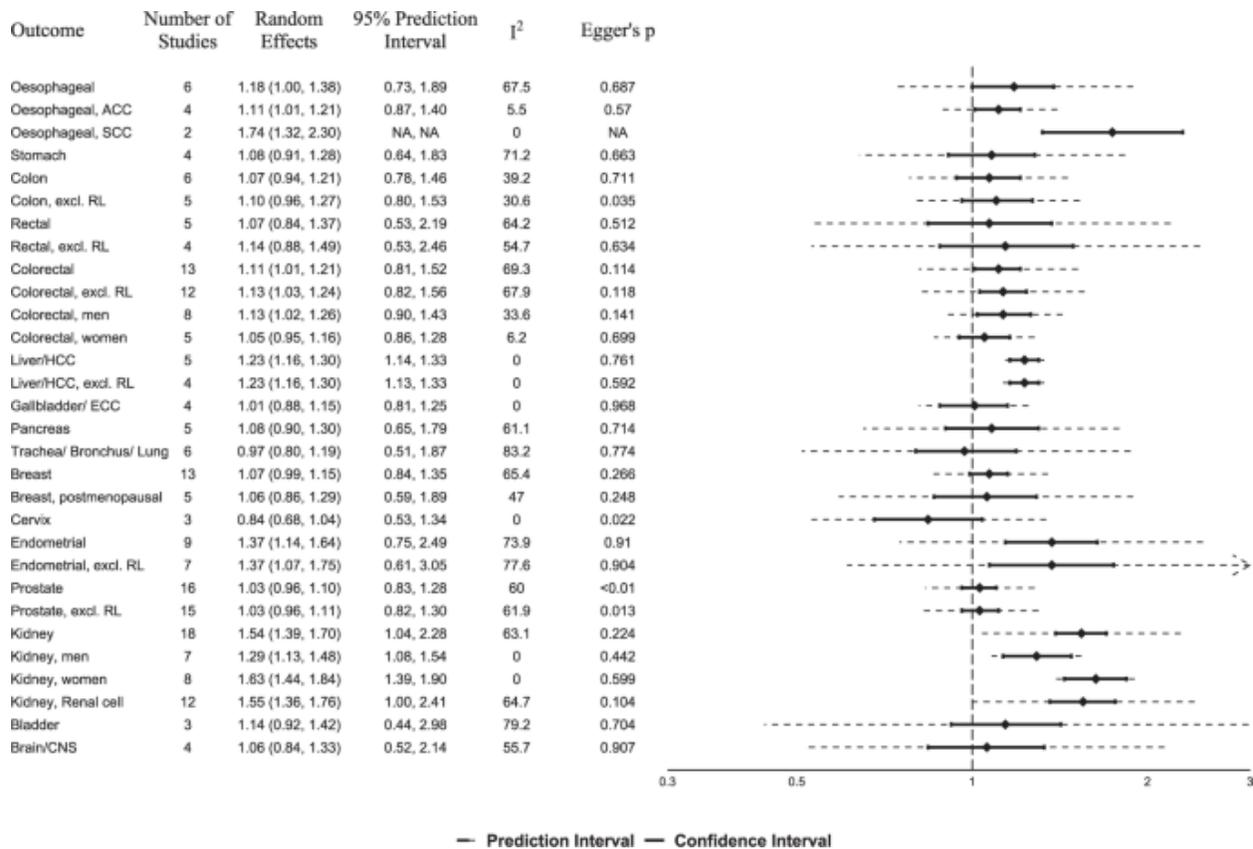


Table 1 derived from <https://www.nature.com/articles/s41598-019-45014-4/figures/2>

Table 2

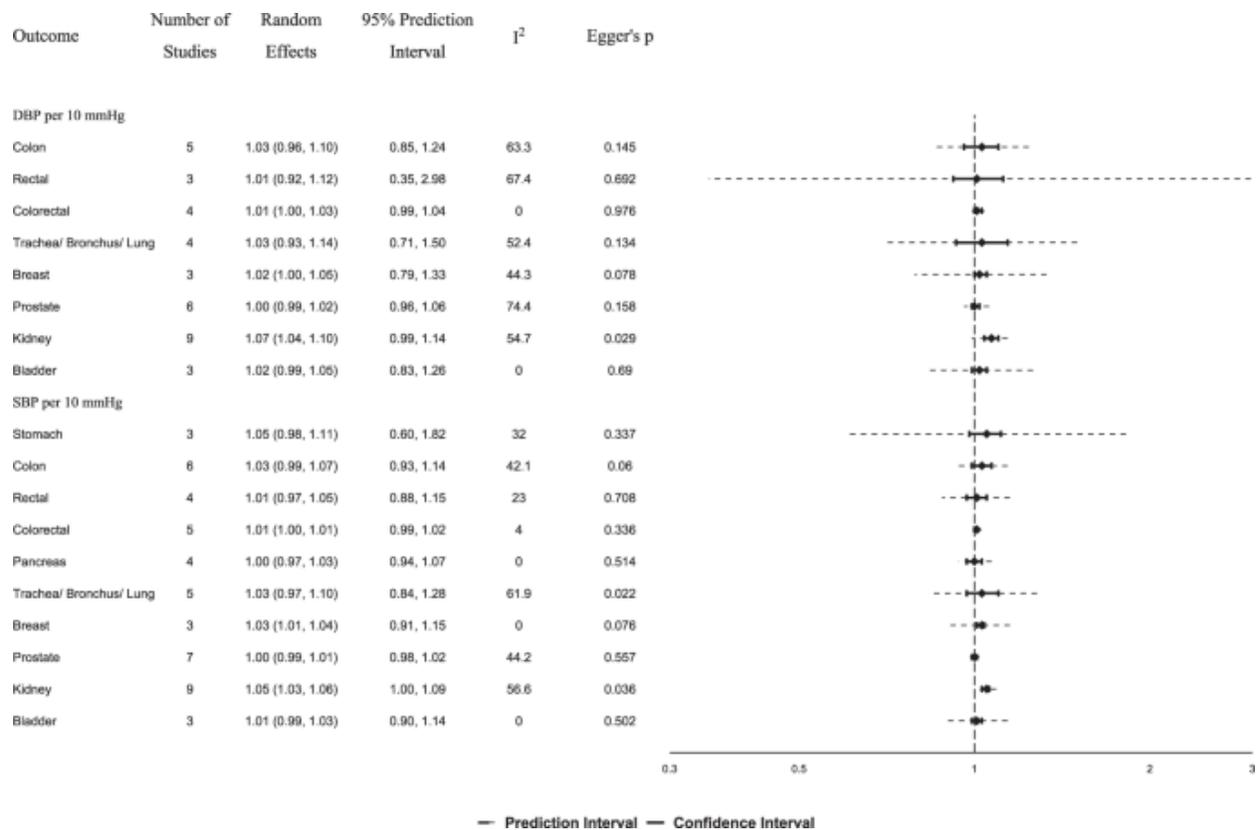


Table 2 derived from <https://www.nature.com/articles/s41598-019-45014-4/figures/3>

We conducted 29 meta-analyses between SBP or DBP and 11 malignancies and 30 meta-analyses between hypertension and 16 distinct cancers for the primary analysis utilizing only prospective studies. Table 1 provides a synopsis of the different effects and the relative risk estimates for cancer in different parts of the body, variability statistics, and tests of the effects of high blood pressure, while Table 2 represents the different types of blood pressure.

The incidence of kidney cancer was shown to be statistically significantly correlated with hypertension in Table 1. Although there was significant heterogeneity, there was no evidence of marginal study effects. Similar results were observed when we meta-analyzed papers showing that only renal cell carcinoma patients were included. Without accounting for between-study

variability within each sex-specific analysis, the link between hypertension and kidney cancer was statistically significant in both women (n = 8 studies) and men (n = 7 studies), with women having considerably higher estimates. Subgroup analyses of prospective studies that accounted for at least age vs. Those that controlled for age and at least three of the five risk factors produced comparable results. In addition, one has to consider factors such as Diet, cancer-causing agents, hormones, and family history (Yassin et al., 2019). The meta-analysis of 14 case-control and prospective studies yielded a summary RR of 1.60.

Discussion

In a systematic assessment of observational data, we found a significant association between hypertensive or high blood sugar and the development of 18 distinct types of cancer. While it was previously established that hypertension raises the risk of kidney cancer, our findings also reveal a relationship between hypertension and the development of the intestine, mammary, endometrial, liver, and esophagus malignancies. Cancers of the esophagus, liver, pancreas, lungs, ovaries, cervix, prostate, bladder, and brain did not exhibit statistically significant relationships.

Over the last few generations, several researches have been conducted to investigate the link between high blood pressure and kidney cancer (Ko et al., 2016). Most of those studies have identified a link between the two, which we defined as a 54% higher risk, with a higher prevalence in females than males (63% vs. 29%) (Lee et al., 2020). The risk of developing kidney cancer was shown to rise by 5 percent for every 10 millimeters of mercury (mm) increase in systolic blood pressure (SBP) and 7 percent for every ten-mmHg increment in diastolic blood pressure (DBP), according to dosage. Previous meta-analyses have revealed similar relationships

(Hidayat et al., 2017). Since risk factors for cancer and hypertension, such as tobacco smoke, obesity, alcohol intake, and physical inactivity, are comparable, it is unclear if this link is causal (Koene et al., 2016). Women suffering from high blood pressure had an increased risk of breast cancer (Pereira et al., 2012).

Many of these possible confounders have not been corrected for in several investigations, but four observational studies that did do so and used a thorough adjustment strategy still revealed significant relationships, as described in the current and prior conceptual (Hidayat et al., 2017). Mendelian random assignment trials and future prospective randomized studies are needed to confirm whether or not the observed association is causal (Dimou & Tsilidis, 2018). Current Mendelian randomized research found that diastolic blood pressure, but not systolic and diastolic blood pressure, was positively related to renal cell cancer (Johansson & Carreras-Torres, 2019). However, it is speculated that the neurobiological mechanisms underlying the link between cardiovascular risk and kidney cancer are progressive kidney potentially life-threatening, oxidative damage, and market liberalization of the adrenal hormones system, in particular the steadily increasing affirmation of aldosterone neurochemicals and the narrow of the insulin-like integrin enzyme (Sobczak et al., 2017).

In addition, we computed a generally positive association between high blood pressure and the risk of hepatocellular carcinoma, with those with hypertension having an 11% increased risk of developing prostate cancer (Hirai et al., 2019). Only four of the 13 prospective studies included in this meta-data analysis set made thorough multivariate modifications, and the possible greater risk for hypertensive participants in those studies was 30% (Dickerman et al., 2018). Another conceptual conducted by Esposito et al. in 2013 utilizing cohort and research studies revealed a 9% rising trend in colorectal cancer attributed to hypertension (Esposito et al.,

2013). To our information, no specific mechanism has been established to relate high blood pressure to colorectal cancer (Samarakoon et al., 2018). However, it has been demonstrated that high blood pressure raises cancer risk by preventing apoptosis. Given the absence of well-designed studies in the literature, recent results should be interpreted with caution.

Hypertension was connected to a 7% increased incidence of all breast cancer in 13 prospective trials. Only five of these investigations used thorough multifactorial modifications, and when hypertensive people were compared to normotensive people, the risk for overall breast cancer was 10%, and the risk for reply disease was 38% (Chuang et al., 2015). These findings are consistent with those of a previous conceptual that Han and his collaborators conducted using data from 12 population studies. In that analysis, they discovered that people with hypertension had a 7% heightened incidence of a whole mammography danger, irrespectively of any improvements decided to make (Han et al., 2017). Several possible explanations for this association include the inhibition of caspase, hypoxia related to target organs, and chronic inflammation that increases the reactive oxygen species produced (Rausch et al., 2017).

According to the prevalent theory, increased blood pressure and the risk of developing esophageal cancer, squamous-cell carcinoma, endometriosis, and liver disease are significantly associated with increased blood pressure. However, this framework included a relatively small number of observational published research that ranged from two for epithelial tissue carcinoma of the digestive tract to 9 for pelvic pain, and a significant proportion of them showed that they were not associated without the required accurate and comprehensive multiple linear regression modifications, attempting to improve severe reservations over the authenticity of Preceding conceptual for uterine cancer did not examine research project design and methodology. Previous conceptual for endometriosis did not evaluate the quality of the studies.

No link was observed between hypertension and stomach, gallbladder, pancreatic, lungs, cervix, sperm, bladder, or brain cancer. New support for high blood sugar levels and the chance of developing prostate cancer used 21 research and longitudinal studies. It found a significant statistical association between the two 8% increased risk. However, this report did not examine individualized learning quality or design. (Liang et al., 2016). The present conceptual advantages include its thorough search method, the inclusion of "metabolic syndrome" in the query optimizer, and detailed susceptibility and subgroup analyses. This work has flaws. First, hypertension and cancer may share risk variables like age, smoking, alcohol intake, nutrition, and obesity.

Unfortunately, most research in this sector did not make complete multivariable adjustments, raising questions regarding the durability of particular study findings even when considering the well-known link between renal cancer and high blood pressure are two of the risks (Kim et al., 2020). Second, most studies did not conduct subgroup analyses by possible effect moderators (such as generally favorable toward prescription use), which may have offered a more accurate assessment of patient subgroup relationships. Third, there is a possibility that some of the associations discovered were due to identification bias. This is because persons with hypertension are more likely to seek medical attention, which may result in earlier cancer discovery. Future longitudinal and Mendelian randomized studies should help estimate correlation variables.

Epidemiological studies of carcinoma of the kidney have linked hypertension to the disease (Carlo et al., 2019). Hypertension increases kidney carcinoma incidence by 1.6-fold, according to a meta-analysis of 18 studies (Xie et al., 2020). Other cancer locations have inconsistent findings. According to Raglan et al. (2019), endometrial cancer was not linked to

hypertensive problems in a case-control study of 469 endometrial cancers in the United States. Women with a family history of hypertension or diabetes mellitus face a threefold greater risk, according to a specific description of 285 cases from a European surgical center (Zargar et al., 2021). Women in their post-menopausal stage also are at a big risk of breast cancer (Guo et al., 2019). Colon, chest, lung, and testicular cancers have inconsistent relationships (Wang et al., 2015). Among Turkish women, breast cancer is prevalent due to their lifestyle (Beji et al., 2007). In Korea, studies have found a huge correlation between medical conditions and breast cancer (Jung et al., 2013).

Our study shows that BP and cancer may be linked through proliferative aberrations in vascular smooth muscle (Puska et al., 2016). Alternatively, abdominal obesity, which Body fat percentage may not have sufficiently adjusted for, may confound the relationship between BP and cardiovascular disease risk. This is the first and most extraordinary study to consider measurement error and found a higher link between high blood pressure and the development of the disease or mortality in men than in women (Berger et al., 2016). The second largest study indicated a link between hypertension and endometrial and renal cancer (Tini et al., 2019). In that study, pancreatic cancer risk was more significant for hypertension women than men, consistent with our 10-mmHg findings (Choi ET AL., 2021).

Our bigger sample size, aging demographic, or lack of hypertension therapy information may explain differences in outcomes. Cancer mortality was more strongly linked to BP than cancer incidence. Cancer kind may explain this disparity. High blood pressure and its dependent components may be more critical for tumor progression than tumor initiation (Kidoguchi et al., 2021). Respondents with high blood pressure may be diagnosed with tumors later because of variations in health service behavior, or the repercussions may be increased by discrepancies

between the diagnosis of cancer and the underlying cause of death (Jones et al., 2018). In addition, we found that men and women with similar body mass index (BMIs) had a similar association between BP and melanoma. Sex hormones, high blood pressure, and cancer are all related to this gender gap. Additional studies are required to understand the impact of hypertension on tumor initiation and development and the significance of hypertension's interactions with other metabolic and carcinogen factors.

Hypertensive people have a greater chance of developing renal, colon, and breast cancer, according to the observational evidence from the literature covering 18 different types of cancer (Sionakidis et al., 2021). However, several meta-analyses only contained a few trials, and many corresponding values were of low or moderate consequence, suggesting that they were impacted by confounding variables due to the clinical intricacy of hypertension and the paucity of data on the putative crosslink between high blood pressure and cancer, the present investigation centered on this condition. The current study also showed that hypertension is a potential carcinogenic risk and that the link between high blood pressure and cancer may be seen across organ-specific cancer locations.

Conclusion

In conclusion, the current research found that people with hypertension had a significantly increased chance of developing kidney, chest, gastrointestinal, endometrium, and bladder malignancies. Even though it is challenging to make a definitive statement about why and how this occurs because of the complex nature of high blood pressure and cancer, this study was able to give comprehensive performance reviews of the potential factors of this identified inter and attempt to enhance our understanding of this occurrence and to provide full details that

may have the possibility of improving preventative and rehabilitative treatments for these conditions.

List of Abbreviations

WHO- World Health Organization

BP -Blood pressure

MR- Mendelian randomization

RR- arterial blood pressure

CI- cardiac index

SBP- systolic blood pressure

DBP- diastolic blood pressure

BMI- body mass index

Declarations

- a) Ethics approval and consent to participate: "Not applicable."
- b) Consent to publish: "Not applicable."
- c) Availability of data and materials: All data and references are available in the Article or "Not applicable."
- d) Competing interests: "The authors declare that they have no competing interests."
- e) Funding: "Not applicable."
- f) Authors' Contributions:

1-Prof Nikolaos Tzenios: Main author, investigation,

2- Dr. Mary Tazanios: interpretation of data

3- Dr. Mohammad Chahine: substantive revision of the final draft

4- Corresponding Author:

Professor Nikolaos Tzenios Ph.D., FRSPH, FRSM, FAAMFM, FWAMS, FMRS, AcIASS, mRSB, DABAAHP¹ 3 Walham Yard, SW61JA, London, UK

Email address: Nicolas@Trccolleges.com

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