## Pericarditis May Signal Occult Cancer

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July 14, 2017

AARHUS, DENMARK — Pericarditis may be a sign of a hidden malignancy, a new study suggests<sup>[1]</sup>. In a Danish cohort study, people had a higher-than-expected risk of being diagnosed with a malignancy—specifically lung cancer, non-Hodgkin lymphoma, and myeloid leukemia—within the first 3 months after developing pericarditis.

"Physicians treating patients with pericarditis should be aware that these patients have an increased occurrence of cancer and should consider whether additional workup is needed to target or rule out cancer," coauthor Dr Hans Erik Bøtker (Aarhus University Hospital Skejby, Denmark) told *theheart.org* | *Medscape Cardiology*.

"While this is most pronounced when pericarditis manifests with pericardial effusion, it is also important to note that the increased risk is not restricted to wet pericarditis," Bøtker said.

The study is published online June 29, 2017 in Circulation.

With this analysis, the researchers, led by Dr Kirstine Kobberøe Søgaard (Aarhus University Hospital Skejby), sought to determine the magnitude of cancer risk in pericarditis patients.

"We know that pericarditis, which is inflammation of the cardiac sac, may be caused by an undetected cancer," Bøtker said. "It is not known, however, whether this is a frequent cause of pericarditis. We wanted to investigate how often pericarditis is associated with cancer."

Pericarditis may be "wet" or "dry," depending on whether or not there is pericardial effusion in the cardiac sac, he noted. "When pericarditis is wet, it is thought to be more frequently associated with cancer, so we also wanted to investigate whether wet pericarditis required particular attention with regard to the presence of cancer."

The researchers cross-linked Danish hospital registries to identify patients without a history of cancer who were admitted to the hospital with a first-time diagnosis of pericarditis between 1994 and 2013.

They then followed patients for a subsequent cancer diagnosis for up to 10 years (mean 6.4 years) after their admission for pericarditis.

Among 13,759 patients with acute pericarditis, 1550 were subsequently diagnosed with cancer.

Compared with the 1070 new cancer diagnoses that would be expected to occur in the general population, those who had pericarditis were 1.5 times more likely to be diagnosed with cancer (overall standardized incidence ratio [SIR] 1.5, 95% CI 1.4–1.5).

This was driven predominantly by increased rates of lung, kidney, and bladder cancer, lymphoma, leukemia, and unspecified metastatic cancer.

Patients with pericardial effusion had the highest incidence rate ratio (SIR=2.1, 95% CI 1.9-2.3).

Among the pericarditis patients, 376 cancers were diagnosed within 3 months of their incident pericarditis diagnosis, which corresponded to an absolute risk of 2.7%. More than half of these cases (n=210; 56%) were lung cancers. Others were lymphoma (n=36 cases), leukemia (n=16 cases), and unspecified metastatic cancers (n=17 cases).

The risk of having a cancer diagnosed during that 3-month time period was approximately 12-fold higher among patients with pericarditis than would be expected in the general population. The 3-month SIR was 12.4 (95% CI 11.2–13.7), which was mainly driven by lung cancer (SIR=65.0, 95% CI 56.5–74.4).

The risk of hematological cancers was also markedly increased during the first 3 months of follow-up. For non-Hodgkin lymphoma, there was a 30-fold increase, and for myeloid leukemia, there was a 49-fold increased risk.

Between 3 and 12 months following an incident pericarditis diagnosis, 123 cancers were diagnosed. This corresponded to a 1-year absolute cancer risk of 3.7% and SIR of 1.5 (95% CI 1.2–1.7) for any cancer.

Pericarditis was also a prognostic factor for cancer patients.

When the researchers compared survival among 1550 patients who had pericarditis before their cancer diagnosis and 7664 cancer patients with no antecedent pericarditis, they found that the 3-month survival was 80% among those with pericarditis and 86% among those without (hazard ratio [HR] 1.5, 95% CI 1.3–1.8).

Similarly, 1-year survival was 65% for those with pericarditis and 70% for those without (1-year HR 1.3, 95% CI, 1.1–1.5).

"These findings indicate that pericarditis may be a first clinical manifestation of a hidden cancer, most frequently lung cancer, lymphoma, leukemia, and unspecified metastatic cancer, and that the risk of having a cancer diagnosed is most pronounced with wet pericarditis, although seen with dry pericarditis," Bøtker said.

"We hope this important information will be implemented in future textbooks in cardiology and that it will increase the awareness of additional diagnostic workup in patients admitted to the hospital with pericarditis," he added.

## **Emerging Interface of Cardiology, Oncology**

"This study highlights the emerging area of the interface between cardiology and oncology," said Dr Michael Fradley (H Lee Moffitt Cancer Center and Research Institute, Tampa, FL), asked for comment on the findings.

"The 2.7% increase in absolute risk is a pretty significant one in the early zero- to 3-month time frame. An important take-home from this study is that newly diagnosed cardiovascular problems such as pericarditis may unmask an indolent or undiagnosed malignancy. But the big question is, is this pericarditis a manifestation of the malignancy, or is it something that leads to more investigation, and thence to identifying the underlying cancer? We don't really get an answer to this question from this study," Fradley said.

A similar link between cardiovascular disease and cancer was found in a study published last year in *JAMA Cardiology* and reported at that time by *theheart.org* | *Medscape Cardiology*. In that study, Dr David Conen (Brigham and Women's Hospital, Harvard Medical School, Boston, MA) and colleagues found a link between new-onset atrial fibrillation and subsequent malignancy in participants of the Women's Health Study.

"There seems to be a correlation between cardiovascular disease and a future diagnosis of cancer. Is it because the cardiovascular disease leads to more diagnostic modalities so that cancers are found, or is there really some sort of correlation?" Fradley noted.

"For example, many argue that perhaps inflammation plays a role; it plays a role in cancer and it plays a role in pericarditis," he said. "Is there some connection between the inflammatory milieu that leads to the connection between the two? These are questions that are not answered by the paper, but what this paper really leads to are additional hypotheses.

"There is some connection here," he concluded. "Now we need to figure out whether this is a manifestation of something that is going on in the body, or is it just allowing us to search more diligently and then find cancer as a result?"

The study was supported by the Danish Cancer Society and by the Program for Clinical Research Infrastructure (PROCRIN) established by the Lundbeck Foundation and the Novo Nordisk Foundation and the Aarhus University Research Foundation. Søgaard, Bøtker and coauthors and Fradley report no relevant financial relationships.

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## References

1. Søgaard KK, Farkas DK, Ehrenstein V, et al. Pericarditis as a marker of occult cancer and a prognostic factor for cancer mortality. *Circulation* 2017; DOI:10.1161/CIRCULATIONAHA.116.024041. Abstract

Medscape Medical News © 2017

Cite this article: Pericarditis May Signal Occult Cancer - Medscape - Jul 14, 2017.

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