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EDITORIAL COMMENT

Pericardiocentesis With Extended Drainage and Colchicine

New Indication for Malignant Pericardial Effusions?*

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Pericardial effusion is a relatively common manifestation in malignancies, often associated with a poor prognosis (1–3). However, a direct cancer involvement of the pericardium has been reported in up to 45% of cases, and up to two-thirds of pericardial effusions are not due to direct cancer invasion (4–8). Secondary or metastatic pericardial invasion is relatively common in solid tumors (lung and breast cancer) and hematological malignancies, whereas primary neoplasms of the pericardium are rare. Pericardial disease may principally develop from direct or metastatic spread of the primary malignancy, or as a complication of systemic tumor treatment (radiotherapy and chemotherapy); the differential diagnosis of the underlying mechanism has an important therapeutic and prognostic impact in terms of either recurrence or survival. The spectrum of malignant pericardial disease may range from asymptomatic pericardial effusion to hemodynamic instability in the setting of cardiac tamponade and constrictive pericarditis.

Despite its clinical impact, little progress has been made in the diagnosis and treatment of this condition. Especially for treatment, there is a great need for new, more efficacious therapies and interventions, to decrease the recurrences of disease, improve the quality of life of patients, and the prognosis, whenever possible.

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In this issue of the *Journal*, Kim et al. (9) reported the outcomes of 445 patients with presumed malignant pericardial effusions who underwent echocardiography-guided pericardiocentesis with drainage associated with anti-inflammatory therapies (ibuprofen 600 mg 3 times daily for 2 weeks then tapered, or prednisolone 0.5 mg/kg/day, or colchicine 0.6 mg twice daily for 2 months) according to clinical judgment.

In this population (median age 57 years, 56% men), 91% of patients had confirmed diagnosis of malignant pericardial effusion (lung cancer was the most common malignancy in 63% of cases), and cardiac tamponade was reported in about 86% of cases. The majority of patients had advanced cancer with metastasis. Echocardiography-guided pericardiocentesis with drainage was successful in 97% of cases, and complications were reported in 1.5% of cases (cardiac perforation requiring surgical repair in most cases in 0.9%, and pneumothorax in 0.4%). During the 2-year follow-up, 26% of patients developed recurrent pericardial effusion and 46% developed constrictive pericarditis. Patients treated with colchicine showed a lower risk of composite events (adjusted hazard ratio: 0.65; 95% confidence interval: 0.49 to 0.87), as well as all-cause death (adjusted hazard ratio: 0.60; 95% confidence interval: 0.45 to 0.81). Colchicine treatment was also consistently associated with a lower composite event rate on propensity score matching.

Overall, the findings of this study are promising, showing that colchicine, after successful pericardiocentesis with pericardial drainage, can

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improve clinical outcomes. The possible explanation of these findings seems related to the anti-inflammatory effects of the drug, as confirmed by subgroup analysis, where patients with elevated C-reactive protein had beneficial effects from colchicine either for the composite endpoint or all cause death. Extended pericardial drainage is thought to reduce pericardial effusion relapse by promoting the adherence of pericardial layers by the triggered inflammatory reaction, and colchicine can attenuate this inflammatory response, which mimics the model of post-cardiac injury syndromes (10–12).

Colchicine is an old anti-inflammatory drug with a known and well-established role for the treatment and prevention of pericarditis (13,14), and could potentially become a new paradigm of treatment for new cardiovascular indications (e.g., acute and chronic coronary syndromes) (15), and beyond (e.g., for coronavirus disease-2019) (16). Colchicine blocks tubulin polymerization, especially interfering with neutrophils, where it is concentrated. Moreover, it is an inhibitor of the NLRP3 inflammasome (a cytoplasmatic complex of proteins assembled and activated by inflammatory states responsible for the activation of pro-interleukin-1 into IL-1) (17).

Overall, the study is interesting and hypothesis-generating, but several limitations should be acknowledged: 1) the single-center, nonrandomized observation study design; 2) the nonstandardized selection of drugs (doses and times) based on physician decision, which could have introduced several biases (e.g., favoring steroids for more severe cases); and 3) the lack of a systematic and comprehensive evaluation of concomitant cancer treatments.

Nevertheless, this study may be helpful for clinical practice, suggesting extended pericardial drainage and colchicine use after pericardiocentesis in these patients, while waiting for the results of new randomized trials specifically designed to verify the efficacy and safety of this approach.

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