Pancreatic cancer–associated thrombosis

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Malignancy is a well-known cause of clinically significant vascular thrombosis, associated with a 7- to 28-fold increase in the risk of venous thromboembolism across all cancers.[1] Pancreatic cancer is among several malignancies with the highest risk of cancer-associated thrombosis (CAT).[2] Nevertheless, current knowledge of CAT is mostly extrapolated from studies involving Western populations. Data from the Chinese population in Hong Kong are limited; therefore, management strategies for such patients remain controversial. The recent study by Chan et al[3] provides some insight regarding this important topic.

The pathogenesis of CAT is usually multifactorial, with contributions from tumour-derived factors and extrinsic factors. Different tumour subtypes have distinct tendencies to express procoagulation molecules such as tissue factors, microparticles, podoplanin, plasminogen activator inhibitor-1, thrombin, and adenosine diphosphate. The presence of these molecules leads to a hypercoagulable state, which is exacerbated by inflammation involving various cytokines and chemokines (eg, tissue necrosis factor alpha, interleukin-1, and vascular endothelial growth factor). In addition to the tumour-derived factors mentioned above, extrinsic factors including vascular obstruction, immobility, anti-cancer therapy, indwelling catheters, and superimposed infection can also contribute to CAT pathogenesis through diverse mechanisms.[4] These factors may be particularly relevant in the setting of pancreatic cancer, considering the central abdominal location of the pancreas and its close proximity to major blood vessels.

Low-molecular-weight heparin has been regarded as the gold-standard pharmacological treatment for CAT, based on the findings of the 2003 CLOT study (Comparison of Low-Molecular-Weight Heparin versus Oral Anticoagulant Therapy for the Prevention of Recurrent Venous Thromboembolism in Patients with Cancer).[5] However, the era of direct oral anticoagulants has arrived. These newer agents have demonstrated non-inferiority in CAT treatment, compared with the gold-standard low-molecular-weight heparin, during multiple pivotal trials such as the Caravaggio study (apixaban),[6] SELECT-D (rivaroxaban),[7] and Hokusai VTE Cancer trial (edoxaban).[8] Multiple international guidelines have endorsed the use of these agents in CAT treatment, along with the conventional low-molecular-weight heparin and the less favourable warfarin.[9-11]

In this issue of the *Hong Kong Medical Journal*, Chan et al[3] reveal that the overall incidence of CAT is approximately 15% in a predominantly Chinese population, which is lower than the reported incidences in Western populations (ie, 20%-40%).[12,13] Multivariable analysis showed that stage IV disease was a significant risk factor for CAT, whereas the presence of CAT and its subsequent treatment did not significantly influence overall survival. The authors suggested that the absence of a survival benefit with CAT treatment was related to the underlying advanced malignancy status, which can lead to a guarded disease prognosis. Additionally, gastrointestinal bleeding (eg, from varices secondary to venous thrombosis, tumour invasion, or haemobilia) may have had a negative impact on survival.

Future studies will be useful in identifying subgroups of patients with pancreatic cancer who may benefit from therapeutic or even prophylactic anticoagulation, along with the characteristics of patients for whom anticoagulation is considered futile or carries an unacceptable risk of bleeding. Explorations of optimal pharmacological treatment approaches should focus on direct oral anticoagulants, considering that patients in the current study were treated between 2010 and 2015, prior to the era of CAT treatment via direct oral anticoagulants. Finally, meaningful insights could be gained by investigating the effects of various pharmacological treatments on patient-reported quality of life measures.

Author contributions

Both authors contributed to the editorial, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

Both authors have declared no conflicts of interest.

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