



REVIEW

Application of Medical Knowledge Graphs in Cardiology and Cardiovascular Medicine: A Brief Literature Review

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ABSTRACT

A knowledge graph is defined as a collection of interlinked descriptions of concepts, relationships, entities and events. Medical knowledge graphs have been the most recent advances in technology, therapy and medicine. Nowadays, a number of specific uses and applications rely on knowledge graphs. The application of the

knowledge graph, another form of artificial intelligence (AI) in cardiology and cardiovascular medicine, is a new concept, and only a few studies have been carried out on this particular aspect. In this brief literature review, the use and importance of disease-specific knowledge graphs in exploring various aspects of Kawasaki disease were described. A vision of individualized knowledge graphs (iKGs) in cardiovascular medicine was also discussed. Such iKGs would

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be based on a modern informatics platform of exchange and inquiry that could comprehensively integrate biologic knowledge with medical histories and health outcomes of individual patients. This could transform how clinicians and scientists discover, communicate and apply new knowledge. In addition, we also described how a study based on the comprehensive longitudinal evaluation of dietary factors associated with acute myocardial infarction and fatal coronary heart disease used a knowledge graph to show the dietary factors associated with cardiovascular diseases in Nurses' Health Study data. To conclude, in this fast-developing world, medical knowledge graphs have emerged as attractive methods of data storage and hypothesis generation. They could be a major and effective tool in cardiology and cardiovascular medicine and play an important role in reaching effective clinical decisions during treatment and management of patients in the cardiology department.

Keywords: Medical knowledge graphs; Advances in therapy; Cardiology; Cardiovascular diseases; Artificial intelligence

Key Summary Points

Medical knowledge graph as a form of artificial intelligence has been among the most recent advances in technology, therapy and medicine.

Through knowledge graphs, data can be viewed in context via linking and semantic metadata; hence, a framework for data integration, unification, analysis and sharing could be provided.

The application of knowledge graphs in cardiology and cardiovascular medicine is a new concept.

In this fast-developing world, medical knowledge graphs have emerged as attractive methods of data storage and hypothesis generation and could be a major and effective tool in cardiology and cardiovascular medicine.

Knowledge graphs could play a major role in making effective clinical decisions during treatment and management of patients in the cardiology department in the near future.

INTRODUCTION

The medical knowledge graph as a form of artificial intelligence (AI) has been among the most recent advances in technology, therapy and medicine [1, 2]. A knowledge graph is defined as a collection of interlinked descriptions of concepts, relationships, entities and events [3]. Through knowledge graphs, data can be viewed in context via linking and semantic metadata; hence, a framework for data integration, unification, analysis and sharing can be provided. Articulating these data as a graph can allow to use graph-based approaches to work with the data. A web of data is created through all of these relationships, and this web of data can be used in computing applications to help them 'think' about medicine the same way as the human brain does.

Knowledge graphs are being used almost everywhere today [4, 5]. An explanation using an example should be sufficient for people to understand this concept even better. When you search the word 'WHO' in Google, for example, a small box called an Infobox will appear at the right hand side of the search result page. This Infobox gives you a quick summary of the World Health Organization, which includes its logo, Google map link, founders, parent organization, subsidiaries and so on. Similarly if you search for a disease like 'coronary artery disease,' Google will show you an even more structured Infobox, which gives you an

overview of the disease, its signs and symptoms, diagnosis, differential diagnoses, treatments and managements. All these data are actually pulled out by Google from its knowledge graph. And all those provided data could serve as direct answers to the questions behind your search.

Nowadays, a number of specific uses and applications rely on knowledge graphs [6, 7]. Examples include data and information services such as intelligent content and package reuse, knowledge graph powered drug discovery, semantic search, advanced drug safety analytics and so on.

Even though AI and machine learning have started to be applied in cardiovascular medicine and interventional cardiology [8, 9], the application of a knowledge graph, another form of AI in cardiology and cardiovascular medicine, is an extremely new concept, and only a few studies have been carried out on this particular aspect. In this brief literature review, we describe the application of knowledge graphs in cardiology and cardiovascular medicine.

LITERATURE SOURCES AND SEARCH STRATEGIES

Literature sources included MEDLINE, EMBASE, Google Scholar, Web of Science and Cochrane Collaboration. Since this research topic is very new and little reported, Google was also searched for relevant abstracts or unpublished papers from conferences.

English publications were searched. The following search terms or phrases were used: “Knowledge graph and cardiovascular diseases;” “Knowledge graph and cardiology;” “Knowledge graph and cardiac;” “Knowledge graph and heart diseases.”

All studies which were based on ‘knowledge graph or its application in cardiology or any cardiac disease’ were considered relevant to this literature review.

The flow chart for study selection is given in Fig. 1.

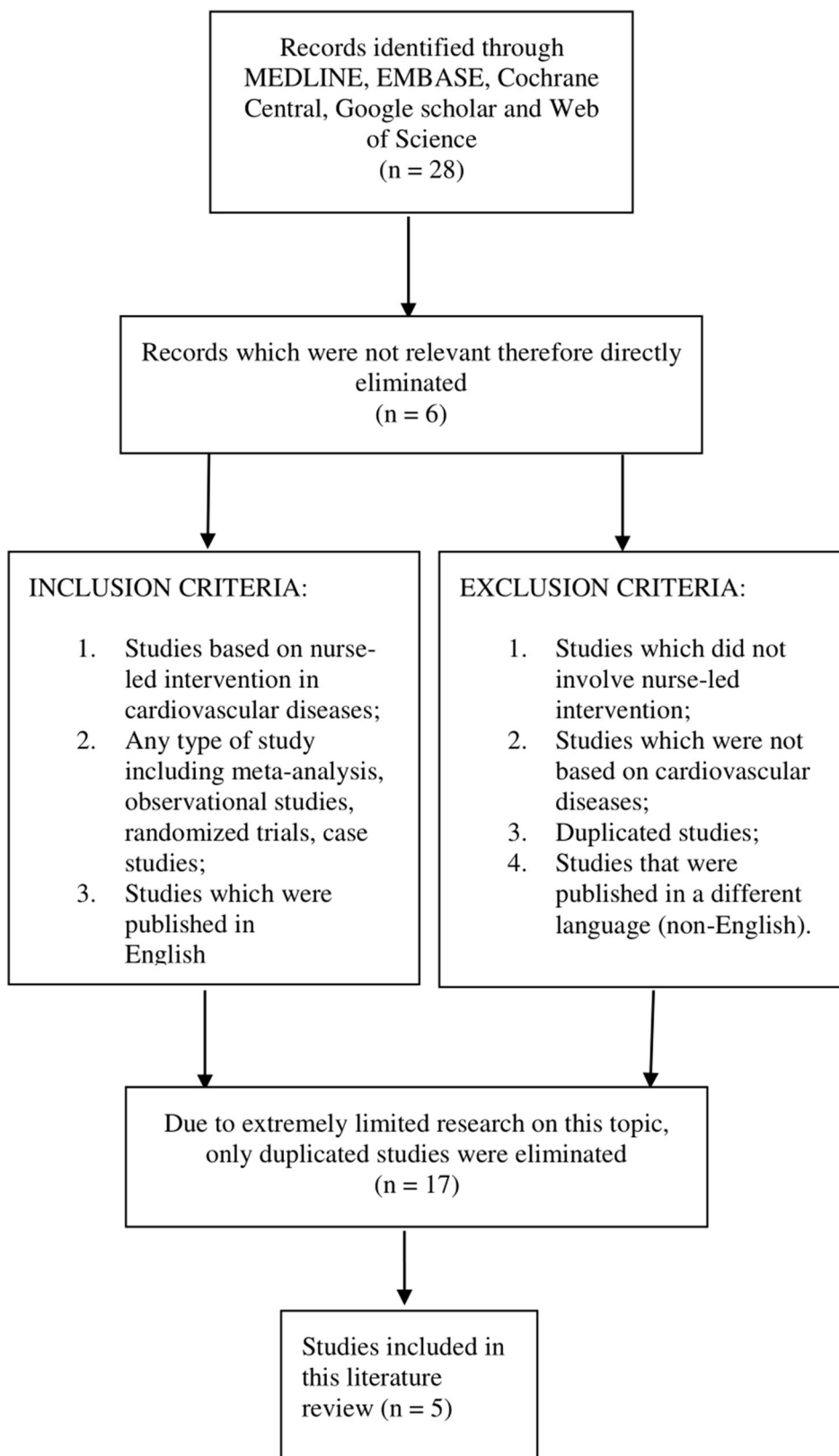
Table 1 defines the purpose of the relevant studies.

COMPLIANCE WITH ETHICAL GUIDELINES

This literature review is based on previously published studies and does not contain any studies with human participants or animals performed by any of the authors.

APPLICATION OF MEDICAL KNOWLEDGE GRAPHS IN CARDIOLOGY AND CARDIOVASCULAR MEDICINE

Despite the extremely limited research on knowledge graphs in cardiology and cardiovascular medicine, we tried to gather information from the available research. A study published in February 2021 [10] demonstrated the use and importance of disease-specific knowledge graphs in exploring various aspects of Kawasaki disease. Kawasaki disease a fatal disease which cause severe physical and mental damage to infants and young children by affecting coronary arteries, causing coronary artery disease in children and also in adulthood. As part of the diagnosis and treatment, various complex knowledge and data resources related to Kawasaki disease need to be analyzed by the treating physicians to acquire information to make effective clinical decisions. Knowledge graphs of Kawasaki disease, also called as Kawasaki disease knowledge graphs (KDKG), consist of a variety of knowledge resources related to Kawasaki disease. The information includes clinical guidelines, clinical trials, medical literature, drug knowledge bases and clinical ontology knowledge bases and so on. Through this knowledge graph of Kawasaki disease, comprehensive knowledge could be effectively transformed into well-structured knowledge. Therefore, corresponding knowledge could be effectively, quickly and accurately obtained to support clinical decisions. The authors clearly demonstrated the application of a knowledge graph in Kawasaki disease, and to illustrate this, they used different cases as examples. For example, the international medical community has not yet found the true cause of Kawasaki



◀ **Fig. 1** Selection of studies for this brief literature review

disease. The question is whether Kawasaki disease is associated with a bacteria or virus. Therefore, through semantic search, which microorganisms have been associated with this coronary disease could be discovered easily and rapidly. Based on this medical knowledge graph on Kawasaki disease, the results showed *Herpes zoster* to be the most frequently mentioned virus followed by Retroviridae. This application of a medical knowledge graph could be a very effective tool in cardiology and cardiovascular medicine in the future.

Another study presented a vision of individualized knowledge graphs (iKGs) in

Table 1 Purpose of the eligible studies which have contributed to this brief literature review

Studies selected for this literature review	Purpose
Huang et al. [10]	Description of the benefits of a knowledge graph based on Kawasaki disease
Ping et al. [11]	A vision of knowledge graphs in cardiovascular medicine
Milanlouei et al. [16]	Specifically focused on the knowledge graph in a study based on the comprehensive longitudinal evaluation of dietary factors associated with acute myocardial infarction and fatal coronary artery disease
Li et al. [17]	Based on a Chinese knowledge graph for cardiovascular disease
Yang et al. [18]	Use of a knowledge graph to analyze neglected influencing factors in statin-induced myopathy in a case of coronary heart disease

cardiovascular medicine [11]. Such iKGs would be based on a modern informatics platform of exchange and inquiry that could comprehensively integrate biological knowledge with medical histories and health outcomes of individual patients. This could transform how clinicians and scientists can discover, communicate and apply new knowledge together. The authors wanted to show that physicians could have their own personal AI assistant to help with individualized patient care strategies. The National Institutes of Health Precision Medicine Initiative Cohort Program presented a knowledge network that used biomedical informatics to bridge basic biological knowledge on molecular disease [12]. Evidence across methods could be linked through this network to characterize a disease process, deal with disease classification, provide more effective treatment solutions and tailor preventive strategies for specific individuals. Current and emerging informatics developments have shaped everyday clinical practice, including echocardiographic pattern recognition [13], Framingham Risk Score [14], and random survival forests to predict survival in systolic heart failure [15].

In a systematic comprehensive longitudinal evaluation of dietary factors associated with acute myocardial infarction and fatal coronary heart disease [16], the authors made use of a knowledge graph to show the dietary factors which were associated with cardiovascular diseases in the Nurses' Health Study data. This knowledge graph was explained by nodes of the graph, which were dietary exposures and cardiovascular diseases, respectively, as two sets of nodes. The studies' association was represented by an edge whose color denoted the direction of the association (whether positive or negative), with different colors to denote positive and negative associations between an exposure and the disease. This knowledge graph was simple and easily understood, providing an aid to clinical decision-making.

Moreover, a conference paper reported that applying a knowledge graph in medicine could yield effective knowledge from medical information and, in combination, could result in structured knowledge which could promote research and application of intelligent diagnosis

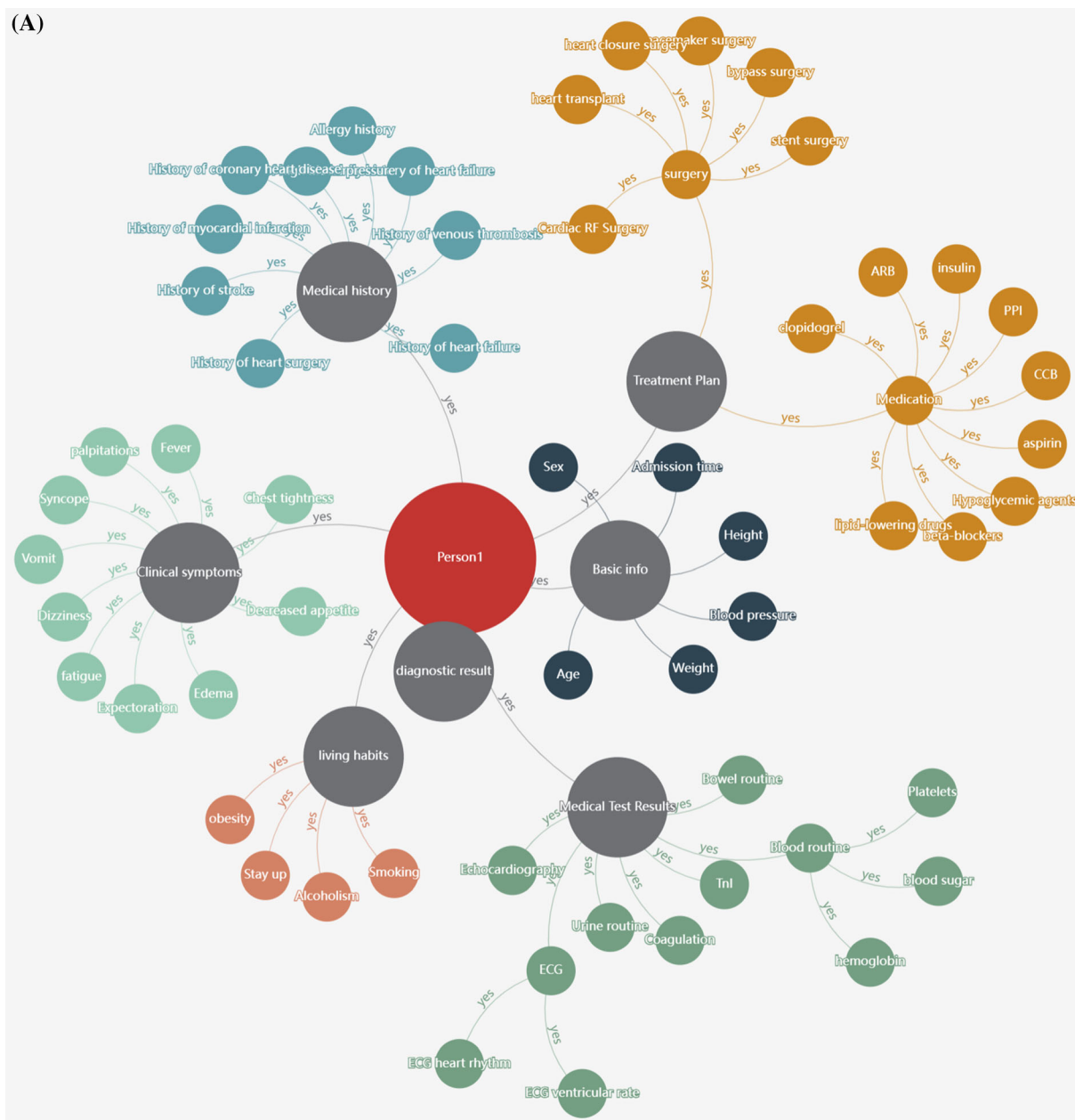


Fig. 2 Illustrations of knowledge graphs in cardiovascular medicine. **A** Knowledge graph of patient A with cardiovascular disease. **B** Knowledge graph of patient A and patient B with the same attributes

and treatment as well as strengthen clinical decisions [17]. The authors stated that the knowledge graph is still in its initial stage, and they wished to explore the construction method of the Chinese knowledge graph for cardiovascular disease. In another International Conference on Brain Informatics [18], authors demonstrated the use of a knowledge graph for

the analysis of neglected influencing factors of statin-induced myopathy in a coronary heart disease case by using this new technology of AI. The authors also stated that knowledge graphs of adverse drug reactions and symptoms could assist physicians in predicting adverse events in the future.

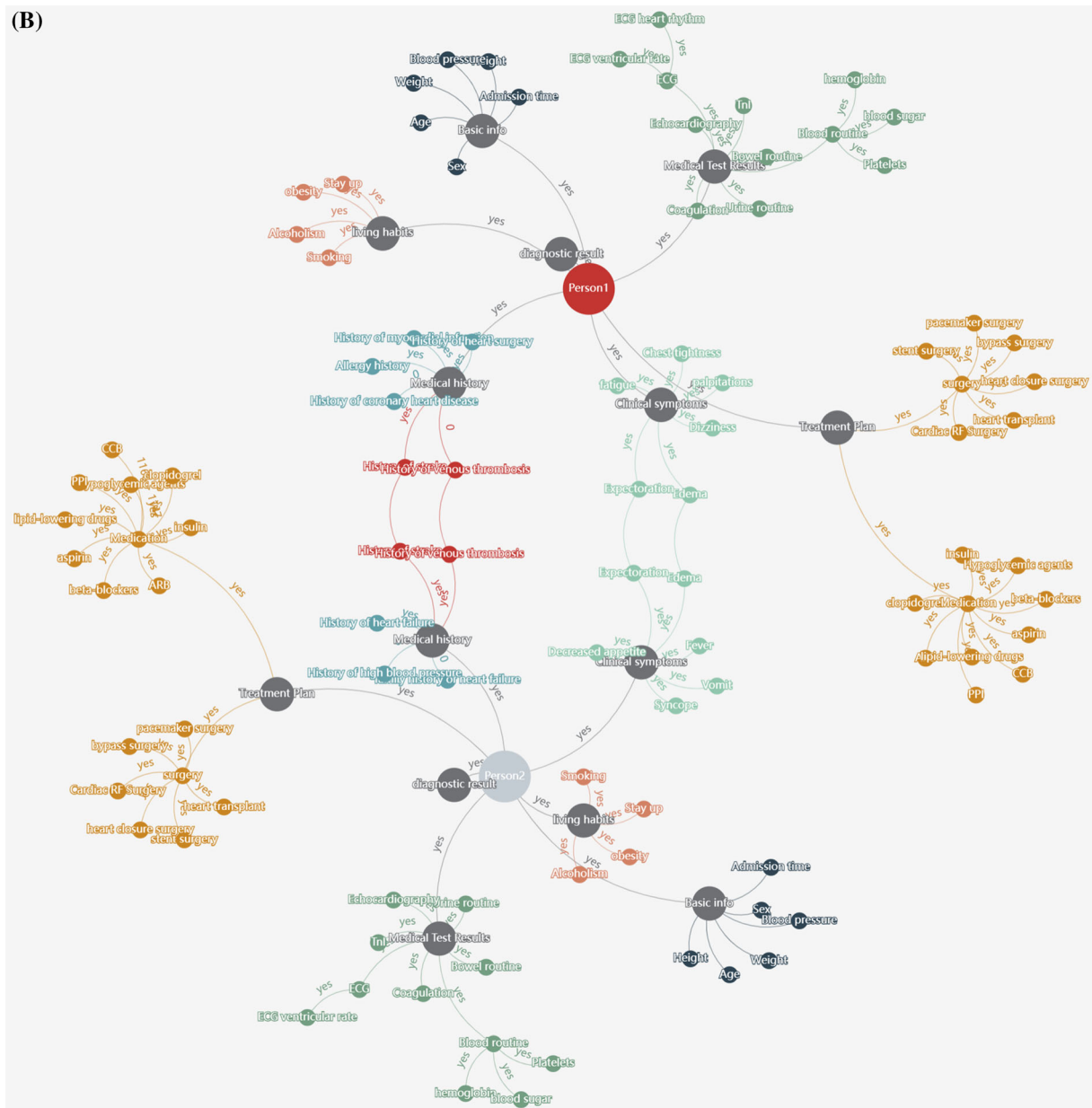


Fig. 2 continued

Finally, even though the knowledge graph is still in its initial stage of development, many publishers now encourage publishers and scientists to supplement their articles with graphical abstracts [19–21], which are pieces of artwork to summarize the main findings of research works, so that readers have a clearer outline of the respective publications. Hopefully, knowledge graphs will follow the same trend in the near future.

DEMONSTRATION OF KNOWLEDGE GRAPHS IN CARDIOVASCULAR MEDICINE

Figure 2 demonstrates two examples of knowledge graphs (Fig. 2A, B) based on patients with cardiovascular disease.

In Fig. 2A, patient A was a patient with cardiovascular disease, and this knowledge graph showed the basic information of the patient, his

clinical symptoms, living habits and lifestyle, diagnostic results, medical history, appropriate medications for this patient, possible available surgeries and the medical test reports.

In Fig. 2B, both patient A and patient B were patients with cardiovascular disease. This knowledge graph showed that both had a history of stroke and venous thrombosis, indicating that they had the same attributes.

CONCLUSIONS

In this fast-developing world, medical knowledge graphs have emerged as an attractive method of data storage and hypothesis generation. They could be a major and effective tool in cardiology and cardiovascular medicine and could play a major role in reaching effective clinical decisions during treatment and management of patients in the cardiology department. This future world will become more interesting with the application of AI in cardiology. Research on AI including knowledge graphs should be encouraged.

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Yongqiang Gao and Jiawang Ding were responsible for the conception and design, drafting the initial manuscript and revising it critically for important intellectual content. Hong Wang wrote the final draft. All the authors approved the final manuscript as it has been written.

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Compliance with Ethics Guidelines. This literature review is based on previously published studies and does not contain any studies with human participants or animals performed by any of the authors.

Data Availability. This is a literature review. No data were used for any statistical analysis. All data shown in this literature review have been published and references have been provided throughout.

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