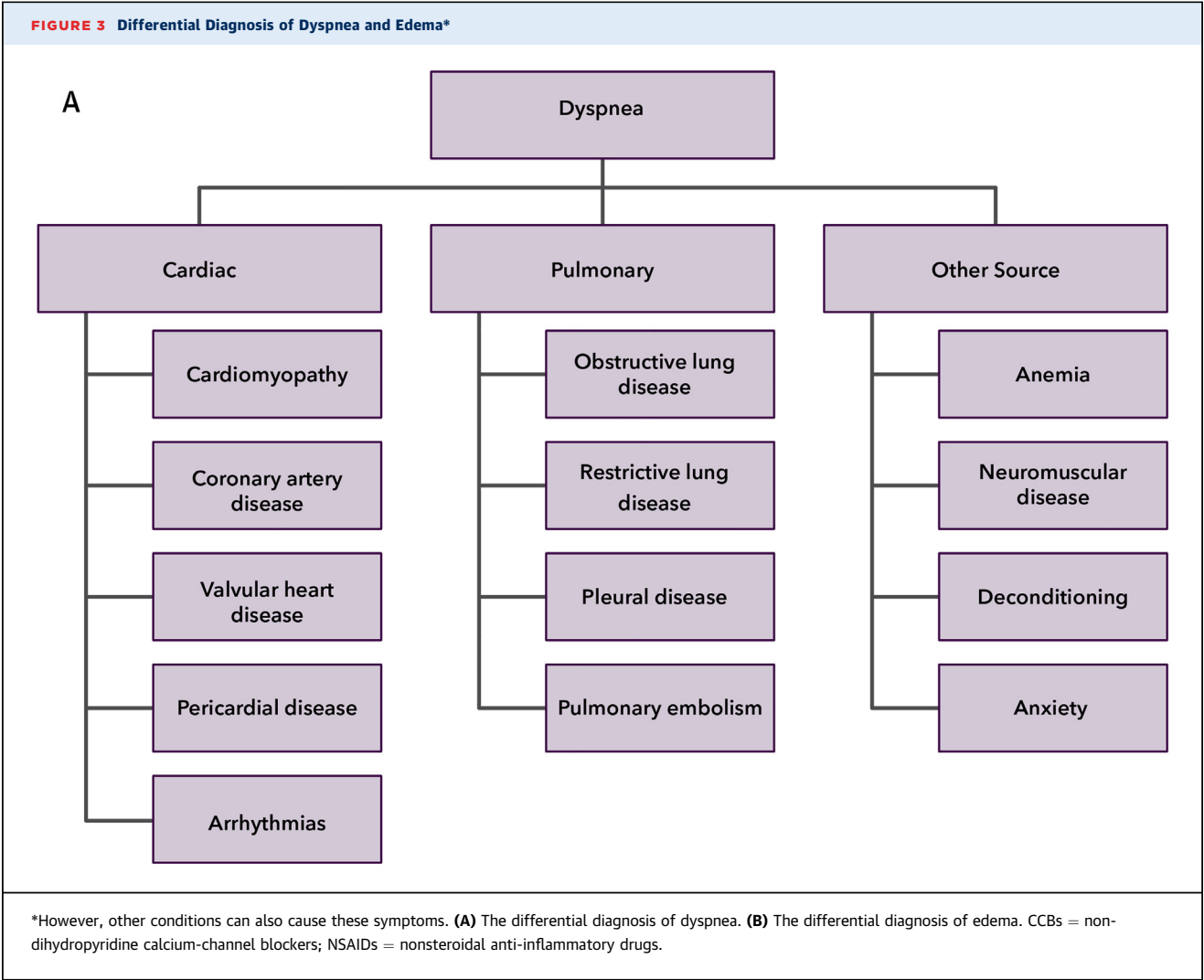




laboratory evaluation, including natriuretic peptides, recognizing that a substantial proportion of individuals with HFpEF have normal natriuretic peptide levels despite unequivocal invasive hemodynamic evidence of HF.¹⁷

6.2. Differential Diagnosis of Dyspnea and Edema

Although dyspnea is a common presenting symptom of HFpEF, it is imperative to consider other causes of dyspnea before assigning the diagnosis. Dyspnea, or shortness of breath, is a frequent cause of emergency visits and hospitalizations across the spectrum of age^{18–20} and can pose a diagnostic challenge given the multiple potential sources of symptoms.²¹

An approach to the differential diagnosis of dyspnea is shown in [Figure 3A](#), organized by cardiac, pulmonary, and other sources. A similar approach can be taken to the differential diagnosis of edema ([Figure 3B](#)),²² although the

first step should be to differentiate edema from lymphedema. Lymphedema is defined as the abnormal accumulation of interstitial fluid and fibroadipose tissue resulting from injury, infection, or congenital abnormalities of the lymphatic system. A history suggestive of risk factors such as lymph node dissection is useful, and lymphedema is most commonly unilateral. A useful physical examination finding to distinguish edema from lymphedema is the Stemmer sign. A positive Stemmer sign is characterized by a thickened skin fold at the base of the second toe or second finger. The examiner’s inability to lift the skin of the affected limb compared with the contralateral limb is considered to reflect fluid accumulation due to lymphedema. However, obesity may cause a false-positive Stemmer sign.^{23,24} Despite being highly sensitive, patients with a negative Stemmer sign and a high clinical suspicion for lymphedema warrant referral for lymphoscintigraphy.