“It’s not just the chemo” – a case of exertional dyspnoea in a Hodgkin survivor.

V Aggelis[1] MRCP

M Westwood[1,2] MBBS MD FRCP FESC

G Lloyd[1] MBBS MD FRCP

S Hallam[3] MA PhD MRCP FRCPath

AK Ghosh[1,2] MBBS MRCP MSc PhD FHEA

1 Department of Cardiology, Barts Heart Centre, St Bartholomew’s Hospital, Barts Health NHS Trust, London, UK

2 Cardio-Oncology Service, Barts Heart Centre, St Bartholomew’s Hospital, Barts Health NHS Trust, London, UK

3 Department of Haemato-Oncology, St Bartholomew’s Hospital, Barts Health NHS Trust, London, UK

It is well established that Hodgkin's lymphoma survivors that have received anthracycline chemotherapy and mediastinal radiotherapy have a higher risk of cardiovascular disease in the form of valvular abnormalities and myocardial dysfunction that emerges several years post treatment [1–3]. We present the case of a 51y old yoga teacher who presented to the Barts Heart Centre Cardio-Oncology Service with progressively deteriorating exertional dyspnoea 13y after treatment of nodular sclerosing Hodgkin lymphoma with anthracycline chemotherapy [5 cycles of ChIVPP/EVA - chlorambucil, vinblastine, procarbazine and prednisolone (ChIVPP) and etoposide, vincristine, and Adriamycin (EVA)] and mantle radiotherapy (35 Gy in 20 fractions). Her past medical history also involved typical endocrine sequelae seen in Hodgkin survivors including hypothyroidism and ovarian failure.

Her echocardiogram demonstrated mild-moderate global impairment of left ventricular (LV) systolic function with a 3D ejection fraction of 47% and a global longitudinal strain of -7.9% (Figure 1). In addition, the aortic valve was calcified resulting in aortic stenosis (AS) (aortic valve area (AVA) of 0.7cm^2 calculated by continuity equation (Figures 2 and 3), mean gradient (MG) 18 mmHg, peak velocity 2.82 m/s). To determine the aetiology of the LV systolic

impairment a cardiac MRI (CMR) scan was arranged which did not show any evidence of LV scar or fibrosis. To determine if this was low flow low gradient (LFLG) severe AS or pseudo-severe AS a dobutamine stress echocardiogram (DSE) was carried out. 10mcg/Kg/min of dobutamine increased stroke volume (32ml/m^2 at rest) by 25% indicating that contractile reserve was present. The MG rose from 19mmHg to 33mmHg and peak velocity from 2.71 m/s to 3.66 m/s. The AVA remained fixed at 0.6cm^2 with a projected valve area of 0.78 cm^2 (0.48cm^2 indexed to body surface area)[4] indicating that this was truly LFLG severe AS.

In view of previous radiotherapy and failed subclavian steal correction, a transcutaneous aortic valve intervention (TAVI) approach was deemed more appropriate than conventional aortic valve replacement surgery.

This case illustrates the need to be aware of the multiple potential late cardiac complications associated with treatment for Hodgkin lymphoma [5]. Our patient developed LV systolic impairment secondary to anthracycline chemotherapy and radiotherapy-induced aortic valve disease combining to cause severe LFLG AS. Appropriate investigations (CMR and DSE) are required in such cases to determine aetiology of systolic dysfunction and severity of AS [6].

References

1 Bijl JM, Roos MM, van Leeuwen-Segarceanu EM, *et al.* Assessment of Valvular Disorders in Survivors of Hodgkin's Lymphoma Treated by Mediastinal Radiotherapy ± Chemotherapy. *Am J Cardiol* 2016;**117**:691–6. doi:10.1016/j.amjcard.2015.11.027

2 van Nimwegen FA, Schaapveld M, Janus CPM, *et al.* Cardiovascular disease after Hodgkin lymphoma treatment: 40-year disease risk. *JAMA Intern Med* 2015;**175**:1007–17. doi:10.1001/jamainternmed.2015.1180

3 Cutter DJ, Schaapveld M, Darby SC, *et al.* Risk of valvular heart disease after treatment for Hodgkin lymphoma. *J Natl Cancer Inst* 2015;**107**. doi:10.1093/jnci/djv008

4 Blais C, Burwash IG, Mundigler G, *et al.* Projected Valve Area at Normal Flow Rate Improves the Assessment of Stenosis Severity in Patients With Low-Flow, Low-Gradient Aortic Stenosis: The Multicenter TOPAS (Truly or Pseudo-Severe Aortic Stenosis) Study. *Circulation* 2006;**113**:711–21. doi:10.1161/CIRCULATIONAHA.105.557678

5 Aleman BMP, van den Belt-Dusebout AW, De Bruin ML, *et al.* Late cardiotoxicity after treatment for Hodgkin lymphoma. *Blood* 2007;**109**:1878–86. doi:10.1182/blood-2006-07-034405

6 Clavel M-A, Magne J, Pibarot P. Low-gradient aortic stenosis. *Eur Heart J* Published Online First: 31 March 2016. doi:10.1093/eurheartj/ehw096

Figures

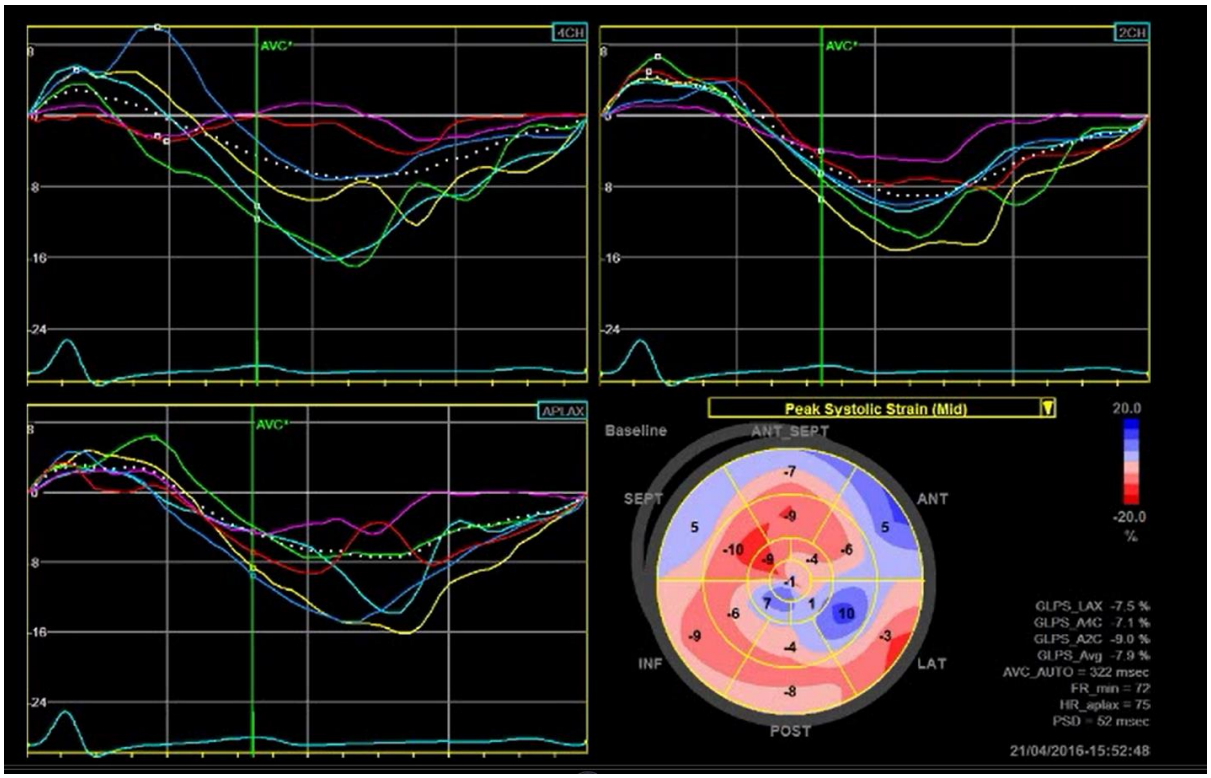

Figure 1. Peak systolic strain maps from the 4 chamber, 2 chamber and apical long axis view and polar plot representing Global Longitudinal Strain.

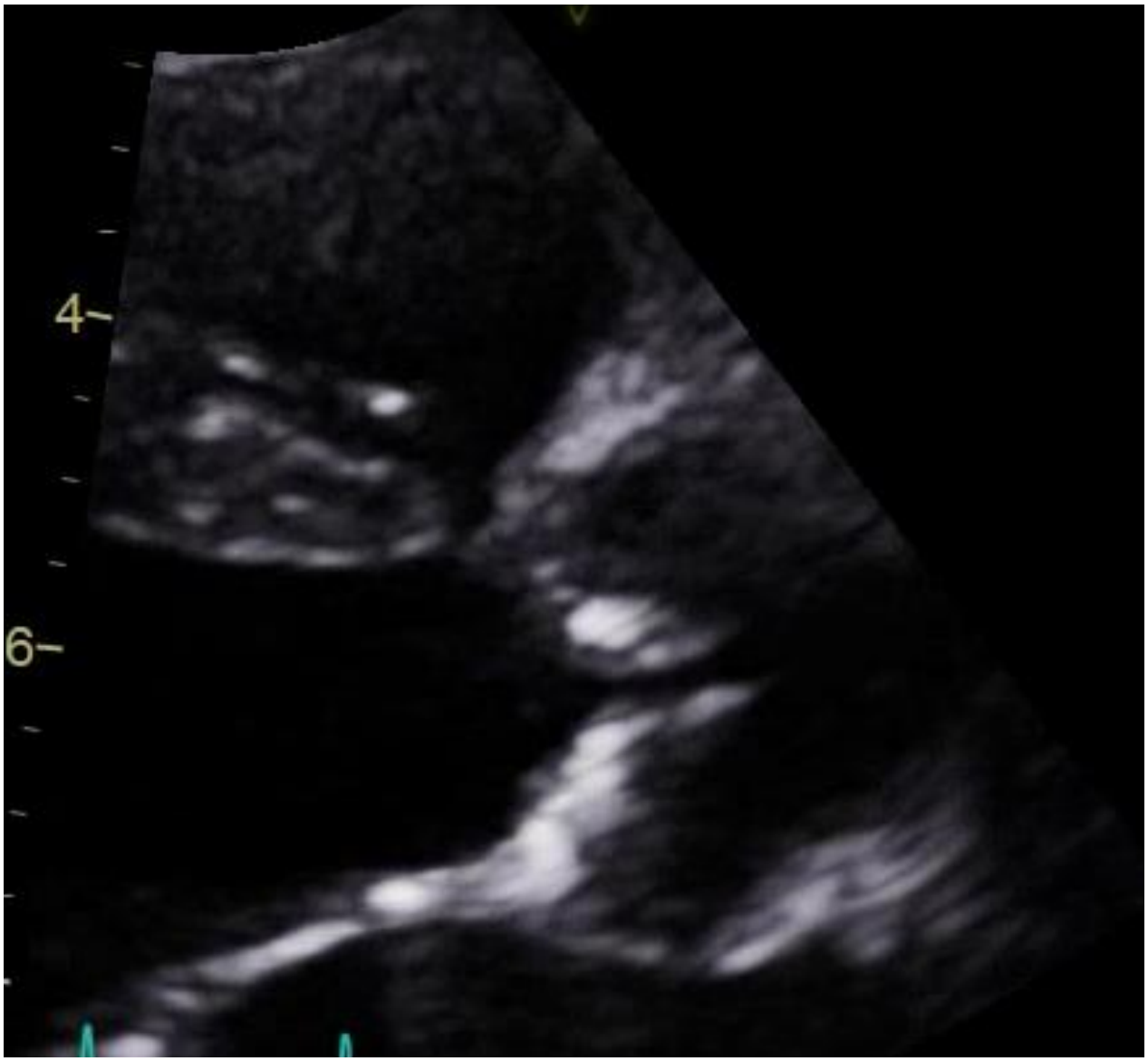

Figure 2. Peak excursion of Aortic Valve during dobutamine stress echocardiogram; parasternal view.

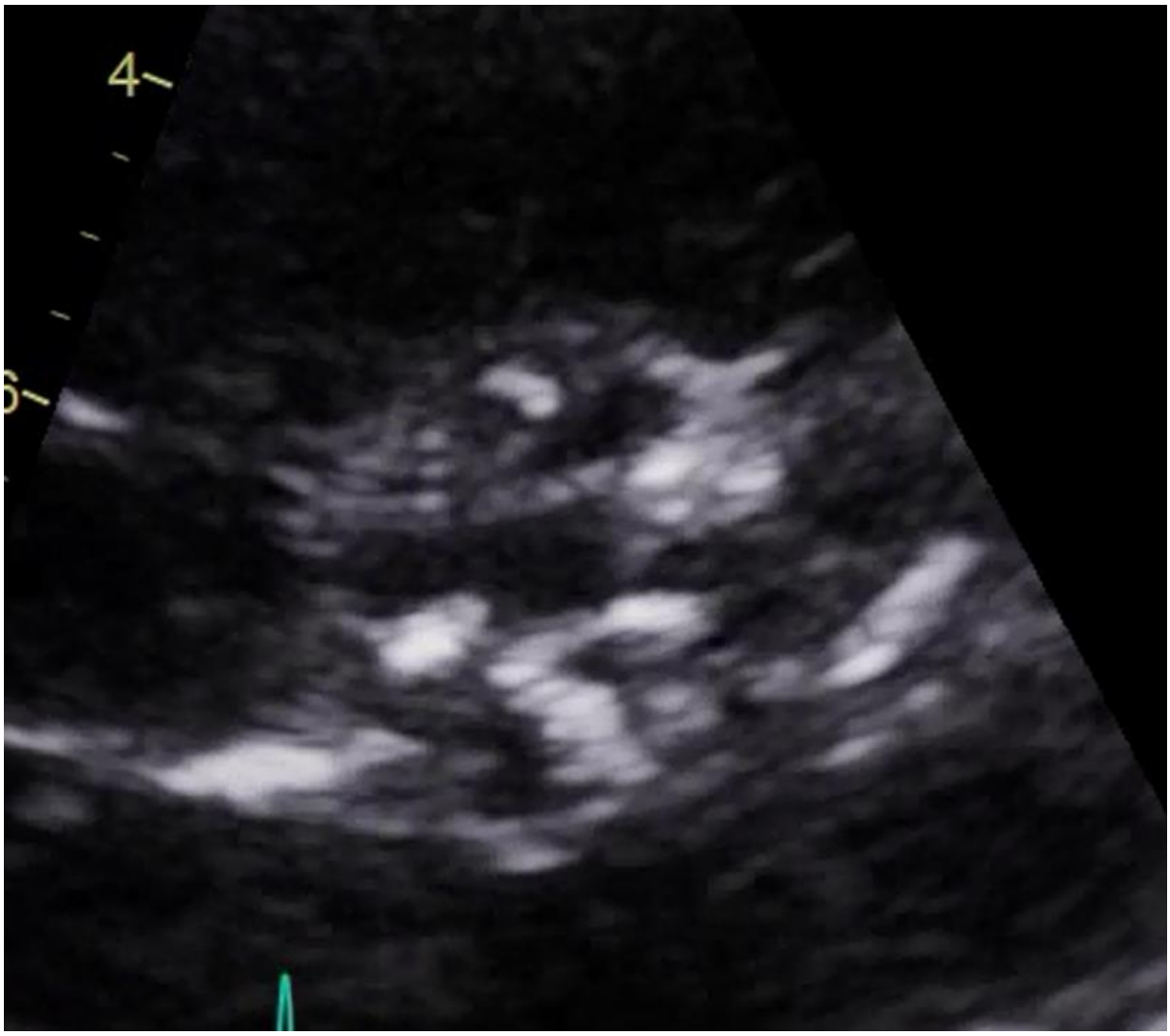

Figure 3. Peak excursion of Aortic Valve during dobutamine stress echocardiogram demonstrating calcified aortic valve; short axis view.