STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	Title page
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3	Abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6	new strategies are required to overcome these limitations and improve outcomes in VT ablation. One potential strategy to overcome these limitations is the use of medical digital twins to guide catheter ablation
Objectives	3	State specific objectives, including any prespecified hypotheses	7	Here, we present a prospective, combined digital twin and clinical VT mapping and ablation study to determine the relationship between invasively defined VT circuits and clinical ablation targets and their respective counterparts observed in the digital twins
Methods				
Study design	4	Present key elements of study design early in the paper	8	Patients requiring catheter ablation for VT were

				prospectively enrolled into this clinical and digital twin study.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8	Patients underwent 3D late gadolinium-enhanced cardiac MRI (LGE-CMR) before the ablation procedure.
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	8	Inclusion requirements included structural heart disease (either ischaemic [ICM] or non-ischaemic [NICM] cardiomyopathy, documented recurrent ventricular tachycardia or implantable cardioverter-defibrillator (ICD) therapy, or prohibitive side-effects from anti-arrhythmic medications
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8	The characteristics of both the digital twins' and the invasively mapped circuits were analysed. Markers of the critical VT isthmus as well as the predicted and invasively delivered RF

				lesions were analysed and the overlap between the digital twins and invasive clinical findings compared
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*8*	The digital twin modelling and VT ablation procedure were each carried out by independent investigators, blinded to the outcome of the opposite modality.
Bias	9	Describe any efforts to address potential sources of bias	11	Coregistration was performed by expert individuals, independent of subsequent analysis and blinded to predicted target site location. The clinical operators were blinded to the digital twin model at all times.
Study size	10	Explain how the study size was arrived at	14	18 patients were recruited into the study.
Continued on next page Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	14	15/18 (83.3%) had ICM and 3/18 (16.7%) had NICM.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	13	Continuous, normally distributed data are expressed as means ± standard deviation. Non-parametric data are expressed as medians ± interquartile range.

				Categorical data is expressed as a percentage. Agreement between clinically observed and digital twin primary predicted VTs was assessed with Cohen's kappa coefficient. The Generalised estimating equation (GEE) method was used to compare predicted site and clinical VT parameters, accounting for repeated measurements from the same individual and controlling for age, sex, aetiology and anti-arrhythmic drug use as co-variates where appropriate
		(*b*) Describe any methods used to examine subgroups and interactions		
		(*c*) Explain how missing data were addressed		
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy		
		(*e*) Describe any sensitivity analyses		
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	14	18 patients were recruited into the study.
		(b) Give reasons for non-participation at each stage		
		(c) Consider use of a flow diagram		
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14	15/18 (83.3%) had ICM and 3/18 (16.7%) had NICM.

				17/18 (94.4%) were male. Baseline left ventricular ejection fraction (LVEF) was 42.3% (± 16.5%).
		(b) Indicate number of participants with missing data for each variable of interest		
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)		
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*14*	During clinical VT ablation, monomorphic VT was inducible in 15/18 (83.3%) patients. 2/18 (11.1%) were not inducible to any ventricular arrythmia, whilst 1/18 (5.6%) was only inducible for VF. A total of 43 VTs were induced in the cohort. The mean number of clinical VTs induced per patient was 2.4 (range 0-6). 14/18 (77.8%) patients had at least one partially mappable VT.
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		
		Cross-sectional study—Report numbers of outcome events or summary measures		
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15	Amongst the 16 VTs where an MDP was detected, sensitivity of predicted target sites to detecting MDPs was 81.3%, with 13/16 MDPs being located within 5mm of a predicted target site
		(*b*) Report category boundaries when continuous variables were categorized		
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		

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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	17	Sensitivity, specificity, positive predictive value and negative predictive value of the digital twin in detecting the critical site of VT (MDP, ECF or termination with ablation) were 81.3%, 83.8%, 21.7% and 98.8% respectively.
Discussion				
Key results	18	Summarise key results with reference to study objectives	19	The main finding of this work is that digital twins' predictions correlate closely to invasively defined critical sites for re-entry and conventional targets for ablation in scar-dependent VT
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	22	This study had several limitations. Coregistration of the MRI-derived model and the EAM was performed manually and, despite considerable care being taken to maximise merge accuracy with multiple fiducial points, some error at the time of merging cannot be excluded.[28] Due to the inherent instability following VT induction, the critical

				isthmus was defined based on presence of diastolic activity (MDPs), with entrainment only possible in a handful of cases. In the absence of entrainment evidence, some areas of diastolic activity may represent bystander regions and not the isthmus itself.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	23	To conclude, we present a combined digital twin and clinical VT ablation study, in which digital twins displayed a high degree of accuracy in predicting the critical isthmus and final ablation targets in a cohort of patients with scar-dependent VT.
Generalisability	21	Discuss the generalisability (external validity) of the study results	23	This validation of digital twin technology marks a major step in the translation of digital twins from research tool to a reliable clinical aid in VT ablation.
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19	MW has received funding through the Advanced Ventricular Arrhythmia Training and Research Project, administered by the St George's Hospital Charity (RES 20 21 001). NT has

	received grant funding from the National Institutes of Health (R01HL166759 and R01HL174440), National Science Foundation grant DMS-2436738, and a grant from the Leducq Foundation. MS and AL have received modest, restricted grants from Abbott Laboratories.

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.