Table 5

Author, date and country	*Patient group*	*Study type (level of evidence)*	*Outcomes*	*Key results*	*Study weaknesses*
Abraham AS *et al*, 1987, Israel	94 patients with proven MI 2.4 g $MgSO_4$ daily for 3 days *v* glucose	PRCT	Incidence of : Ventricular triplets R-on-T VT VF Total of above	 8 *v* 13% p=NS 0 *v* 2% p=NS 7 *v* 15% p=NS 0 *v* 4% p=NS 14 *v* 34% p=0.05	Analysed by group sequential design (interim analysis)
Ro *e C et al, 1994, UK*	2316 patients with suspected MI 8 mmol $MgSO_4$ stat and 65 mmol over 24 h *v* equal volume of saline	PRCT	Odds ratio (95% CI) VF VT SVT AF Heart block Sinus bradycardia	 0.74 (0.46,1.20) p=NS 0.87 (0.63,1.20) p=NS 0.69 (0.38,1.26) p=NS 0.92 (0.69,1.23) p=NS 1.17 (0.83,1.65) p=NS 1.38 (1.03,1.85) p=0.02	Clinical significance of arrhythmias not described
Bhargava B *et al*, 1995, India	78 patients with proven MI 73 mmol $MgSO_4$ over 24 h *v* saline	PRCT	Incidence of : Sustained VT Non-sustained VT VF SVT Bradycardia Asystole Mortality at 28 days In hospital mortality	 10 *v* 20% p=NS 23 *v* 50% p<0.02 5 *v* 8% p=NS 0 *v* 6% p=NS 5 *v* 3% p=NS 0 *v* 3% p=NS None 7.5 *v* 8% p=NS	Small numbers
ISIS-4 investigators, 1995, multinational	58 050 patients 80 mmol mg over 24 h *v* no infusion	PRCT	Incidence of : VF Other cardiac arrest 2nd or 3rd degree heart block Heart failure Cardiogenic shock profound hypotension 5 week mortality	 3.5 *v* 3.8% 3.2 *v* 2.9% 3.9 *v* 3.7% 0.01<p<0.05 17.8 *v* 16.6% p<0.001 4.6 *v* 4.1% p<0.01 16.8 *v* 15.1% p<0.0001 7.64 *v* 7.24% p=NS	
Gyamlani G *et al*, 2000, India	100 patients with proven MI 50 mmol mg in 1st 24 h then 12 mmol mg in next 24 h *v* glucose	PRCT	Incidence of : SVT Sustained VT Non-sustained VT VF Total arrhythmias Mortality	 2 *v* 8% p=NS 2 *v* 10% p=NS 4 *v* 12% p=NS 0 *v* 4% p=NS 8 *v* 34% p<0.01 4 *v* 20% p<0.05	Small numbers

SimpliRed and diagnosis of deep venous thrombosis

Report by Steve Jones, *Clinical Research Fellow*
Search checked by Magnus Harrison, *Clinical Research Fellow*

Clinical scenario

A patient attends the emergency department with signs and symptoms consistent with a deep venous thrombosis. Somebody suggests that there is a new bedside blood test, called SimpliRed, that may help to rule out the diagnosis in your patient. You know that ruling out a diagnosis is possible by having a test with a high sensitivity or negative predictive value. You wonder what evidence there is to suggest that SimpliRed fulfils these criteria?

Three part question

In a [patient with a suspected DVT] does the [SimpliRed test] reliably [rule out the diagnosis]?

Search strategy

Medline 1966–11/00 using the OVID interface. [(exp thrombosis or exp venous thrombosis or thrombosis.mp OR venous thrombosis.mp deep venous thrombosis.mp) AND (exp fibrin fibrinogen degradation products or simplired.mp OR d-dimer$.mp)] LIMIT to human and english language OR Medline 1966–11/00 using the OVID interface. simplired.mp.

Search outcome

Altogether 741 and 37 papers found of which 13 were relevant and of sufficient quality. These 13 remaining papers are shown in table 6.

Comments

The "gold standard" investigation for DVT is contrast venography. This has now been replaced in many centres with a strategy of single or serial compression ultrasound, hence the use of different reference standard tests.

If an investigation is to be used in order to rule out a diagnosis, then it must have a sensitivity of 95% or above. In some of the studies mentioned this is the case, however such is the variability of the results obtained in the other studies the safety of SimpliRed as a lone exclusionary test must be in question. The reasons for this variability may include the operators of the assay or the various techniques used. Many of the results however are still inadequate.

Clinical bottom line

It is not safe to use SimpliRed as a lone exclusionary test for a patient presenting to the emergency department with a possible DVT.

Table 6

Author, date and country	*Patient group*	*Study type (level of evidence)*	*Outcomes*	*Key results*	*Study weaknesses*
Wells PS *et al*, 1995, Canada	214 consecutive patients referred for investigation of ?DVT.	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	25% 88% (CI 77, 96) 77% (CI 63, 80) 95% (CI 89, 98) 0.16	No sample size calculation Excluded patients with inconclusive venograms or plethysmogram
Brenner B *et al*, 1995, Israel	86 consecutive patients referred for investigation of ?DVT	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	58% 94% 61% 88% 0.1	Small patient numbers. No sample size calculation. No confidence intervals
Turkstra F *et al*, 1996, Netherlands	234 consecutive patients referred for ?DVT or ?PE	Prospective cohort	Prevalence Sensitivity Specificity NPV	27% 100% (CI 95, 100) 58% (CI 50, 65) 100% (CI 96, 100)	No sample size calculation (but good numbers)
Janssen MC *et al*, 1997, Netherlands	132 patients referred to ED or OPD for investigation of ?DVT	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	67% 61% (CI 51, 71) 90% (CI 81, 99) 52% (CI 29, 75) 0.43	No sample size calculation. Technique of assay may have affected results. Reference standard not applied to all patients
Ginsberg FS *et al*, 1997, Canada	398 consecutive patients referred to thromboembolic OPD as first episode of ?DVT	Prospective management study	NPV D-dimer alone NPV D-dimer and plethysmography together	97.1% (CI 94.5, 98.8) 98.5% (CI 96.3, 99.6)	No sample size calculation. Reference standard not applied to all patients
Mayer W *et al*, 1997, Austria	108 consecutive patients referred to vascular laboratory as ?DVT	Prospective cohort	Prevalence Sensitivity Specificity NPV	31% 100% (CI 89, 100) 75% (CI 63, 84) 100% (CI 94, 100)	Small patient numbers. No sample size calculation. Used single ultrasound as reference standard
Wildberger JE *et al*, 1998, Germany	250 consecutive patients referred for venography	Prospective cohort	Sensitivity Specificity NPV NLR	96% 59% 97% 0.06	No sample size calculation. Patient selection bias. No confidence intervals
Wells PS *et al*, 1998, Canada	496 consecutive outpatients referred with ?DVT	Prospective cohort	Overall sensitivity Overall specificity NPV NLR *Low pretest probability* Sensitivity Specificity NPV NLR *Medium pretest probability* Sensitivity Specificity NPV NLR *High pretest probability* Sensitivity Specificity NPV NLR	94% 71% 98% (CI 96, 99) 0.08 87% 76% 99% (CI 97, 100) 0.17 89% 64% 97% (CI 90, 99) 0.17 98% 54% 86% (CI 42, 97) 0.04	No sample size calculation. Patient selection bias. No confidence intervals
Mauron T *et al*, 1998, Switzerland	45 consecutive outpatients referred with ?DVT.	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	33% 53% (CI 28, 78) 70% (CI 54, 86) 75% (CI 59, 91) 0.67	Small patient numbers. No sample size calculation. Wide confidence intervals
Carter CJ *et al*, 1999, Canada	200 consecutive patients referred to diagnostic radiology department with ?DVT. Inpatients and outpatients	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	28% 87% (CI 80, 96) 79% 94% 0.16	No sample size calculation. Used single ultrasound as reference standard. Wide confidence intervals
Lennox AF *et al*, 1999, UK	200 consecutive patients referred to diagnostic radiology department with ?DVT. Inpatients and outpatients	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	23% 91% 82% 97% 0.11	No sample size calculation. Incorrect test procedure likely to give falsely high sensitivities. No confidence intervals
Farrell S *et al*, 2000, USA	173 consecutive patients referred to ED with ?DVT (48) or ?PE (125)	Prospective clinical trial	Prevalence Sensitivity NPV NLR	33% 56% (CI 32, 81) 77% (CI 62, 92) 0.61 (CI 0.34, 1.11)	Did not recruit all patients required. Used single ultrasound as reference standard. Wide confidence intervals
Van der Graaf F *et al*, 2000, Netherlands	112 outpatients referred to department	Prospective cohort	Prevalence Sensitivity Specificity NPV Likelihood ratio for negative result (NLR)	50% 80% (CI 66, 90) 94% (CI 83, 99) 82% (CI 70, 91) 0.21	Small patient numbers. No sample size calculation. Wide confidence intervals

NPV = Negative predictive value, NLR = Likelihood ratio for negative result.

1 Wells PS, Brill-Edwards P, Stevens P, *et al*. A novel and rapid whole-blood assay for D-dimer in patients with clinically suspected deep vein thrombosis. *Circulation* 1995;**91**:2184–7.
2 Brenner B, Pery M, Lanir N, *et al*. Application of a bedside whole blood D-dimer assay in the diagnosis of deep vein thrombosis. *Blood Coagul Fibrinolysis* 1995;**6**:219–22.
3 Turkstra F, van Beek EJ, ten Cate JW, *et al*. Reliable rapid blood test for the exclusion of venous thromboembolism in symptomatic outpatients. *Thromb Haemost* 1996;**76**:9–11.
4 Janssen MC, Heebels AE, de Metz M, *et al*. Reliability of five rapid D-dimer assays compared to ELISA in the exclusion of deep venous thrombosis. *Thromb Haemost* 1997;**77**:262–6.

5 Ginsberg JS, Kearon C, Douketis J, *et al*. The use of D-dimer testing and impedance plethysmographic examination in patients with clinical indications of deep vein thrombosis. *Arch Intern Med* 1997;**157**:1077–81.
6 Mayer W, Hirschwehr R, Hippmann G, *et al*. Whole-blood immunoassay (SimpliRED) versus plasma immunoassay (NycoCard) for the diagnosis of clinically suspected deep vein thrombosis. *Vasa* 1997;**26**:97–101.
7 Wildberger JE, Vorwerk D, Kilbinger M, *et al*. Bedside testing (SimpliRED) in the diagnosis of deep vein thrombosis. Evaluation of 250 patients. *Invest Radiol* 1998;**33**:232–5.
8 Wells PS, Anderson DR, Bormanis J, *et al*. SimpliRED D-dimer can reduce the diagnostic tests in suspected deep vein thrombosis. [Letter]. *Lancet* 1998;**351**:1405–6.
9 Mauron T, Baumgartner I, Z'Brun A, *et al*. SimpliRED D-dimer assay: comparability of capillary and citrated venous whole blood, between-assay variability, and performance of the test for exclusion of deep vein thrombosis in symptomatic outpatients. *Thromb Haemost* 1998;**79**:1217–19.
10 Carter CJ, Serrano K, Breen DJ, *et al*. Rapid fibrin D-dimer testsfor deep venous thrombosis: factors affecting diagnostic utility. *J Emerg Med* 1999;**17**:605–10.
11 Lennox AF, Delis KT, Serunkuma S, *et al*. Combination of a clinical risk assessment score and rapid whole blood D-dimer testing in the diagnosis of deep vein thrombosis in symptomatic patients. *J Vasc Surg* 1999;**30**:794–803.
12 Farrell S, Hayes T, Shaw M. A negative SimpliRed D-dimer assay result does exclude the diagnosis of deep venous thrombosis or pulmonary embolus in emergency department patients. *Ann Emerg Med* 2000;**35**: 121–5.
13 van der Graaf F, van den Borne H, van der Kolk, *et al*. Exclusion of deep venous thrombosis with D-dimer testing—comparison of 13 D-dimer methods in 99 outpatients suspected of deep venous thrombosis using venography as reference standard. *Thromb Haemost* 2000; **83**:191–8.

Monophasic or biphasic defibrillation

Report by Russell Boyd, *Consultant*
Search checked by Angaj Ghosh, *Senior Clinical Fellow*

Clinical scenario
You have just finished an unsuccessful cardiac resuscitation in a patient who had an initial presenting rhythm of ventricular fibrillation. You wonder if one of the new biphasic defibrillators would have increased the possibility of successful defibrillation.

Three part question
In [an adult patient with ventricular fibrillation] is [biphasic or monophasic D/C shock] better [at restoring sinus rhythm]?

Search strategy
Medline 1966–11/00 using the OVID interface. (biphasic.mp OR monophasic.mp) AND (exp.defibrillation OR exp electric counter shock OR cardioversion.mp).

Search outcome
Altogether 316 papers found of which 313 were irrelevant or of insufficient quality. The remaining three papers are shown in table 7.

Comments
There is some laboratory evidence that biphasic defibrillation has higher first shock success rates for defibrillation of VF/VT. A theoretical advantage exists with biphasic devices but there is no clinical evidence of increased survival in cardiac arrest occurring outside the cardiac arrhythmia laboratory.

Clinical bottom line
The advantages of biphasic devices are currently mainly theoretical. No real world data exist that would suggest an immediate conversion to using biphasic devices.

1 Greene HL, DiMarco JP, Kudenchuk PJ, *et al*. Comparison of monophasic and biphasic defibrillating pulse waveforms for transthoracic cardioversion. *Am J Cardiol* 1995;**75**:1135–9.
2 Mittal S, Ayati S, Stein K, *et al*. Comparison of a novel rectilinear biphasic waveform with a damped sine wave monophasic waveform for transthoracic ventricular defibrillation. *J Am Coll Cardiol* 1999;**34**:1595–601.
3 Bardy G, Marchlinski F, Arjun D, *et al*. Multi-center comparison of truncated biphasic shocks and standard damped sine wave monophasic shocks for transthoracic ventricular defibrillation. *Circulation* 1996;**94**:2507–14.

Table 7

Author, date and country	*Patient group*	*Study type (level of evidence)*	*Outcomes*	*Key results*	*Study weaknesses*
Greene HL *et al*, 1995, USA	171 patients undergoing electrophysiological studies for ventricular arrhythmias with induced VT and VF requiring external defibrillation. Monophasic *v* biphasic	PRCT	Success of first shock in VT	85.2% (75/88) *v* 97.6% (81/83)	Laboratory conditions for fresh arrhythmias
			Success of first shock in VF	78.6% (22/28) *v* 100% (25/25)	
Mittal S *et al*, 1999, USA	184 patients undergoing electrophysiological testing for ventricular arrhythmias producing an induced VF Monophasic *v* biphasic	PRCT	Success of first shock	93% (80/86) *v* 99% (97/98) (p=0.05)	Laboratory conditions for fresh arrhythmias
Bardy G *et al*, 1996, USA	294 patients with induced VF/VT during implantation of cardioversion devices Monophasic *v* biphasic	PRCT	Success of first shock	86% (143/166) *v* 86% (144/167)	Laboratory conditions for fresh arrhythmias Results for VF and VF combined