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CLINICAL RESEARCH

Techniques improving electrical cardioversion success for patients with atrial fibrillation: a systematic review and meta-analysis

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Aims

Electrical cardioversion is commonly used to restore sinus rhythm in patients with atrial fibrillation (AF), but procedural technique and clinical success vary. We sought to identify techniques associated with electrical cardioversion success for AF patients.

Methods and results

We searched MEDLINE, EMBASE, CENTRAL, and the grey literature from inception to October 2022. We abstracted data on initial and cumulative cardioversion success. We pooled data using random-effects models. From 15 207 citations, we identified 45 randomized trials and 16 observational studies. In randomized trials, biphasic when compared with monophasic waveforms resulted in higher rates of initial [16 trials, risk ratio (RR) 1.71, 95% CI 1.29–2.28] and cumulative success (18 trials, RR 1.10, 95% CI 1.04–1.16). Fixed, high-energy (≥200 J) shocks when compared with escalating energy resulted in a higher rate of initial success (four trials, RR 1.62, 95% CI 1.33–1.98). Manual pressure when compared with no pressure resulted in higher rates of initial (two trials, RR 2.19, 95% CI 1.21–3.95) and cumulative success (two trials, RR 1.19, 95% CI 1.06–1.34). Cardioversion success did not differ significantly for other interventions, including: antero-apical/lateral vs. antero-posterior positioned pads (initial: 11 trials, RR 1.16, 95% CI 0.97–1.39; cumulative: 14 trials, RR 1.01, 95% CI 0.96–1.06); rectilinear/pulsed biphasic vs. biphasic truncated exponential waveform (initial: four trials, RR 1.11, 95% CI 0.91–1.34; cumulative: four trials, RR 0.98, 95% CI 0.89–1.08) and cathodal vs. anodal configuration (cumulative: two trials, RR 0.99, 95% CI 0.92–1.07).

Conclusions

Biphasic waveforms, high-energy shocks, and manual pressure increase the success of electrical cardioversion for AF. Other interventions, especially pad positioning, require further study.

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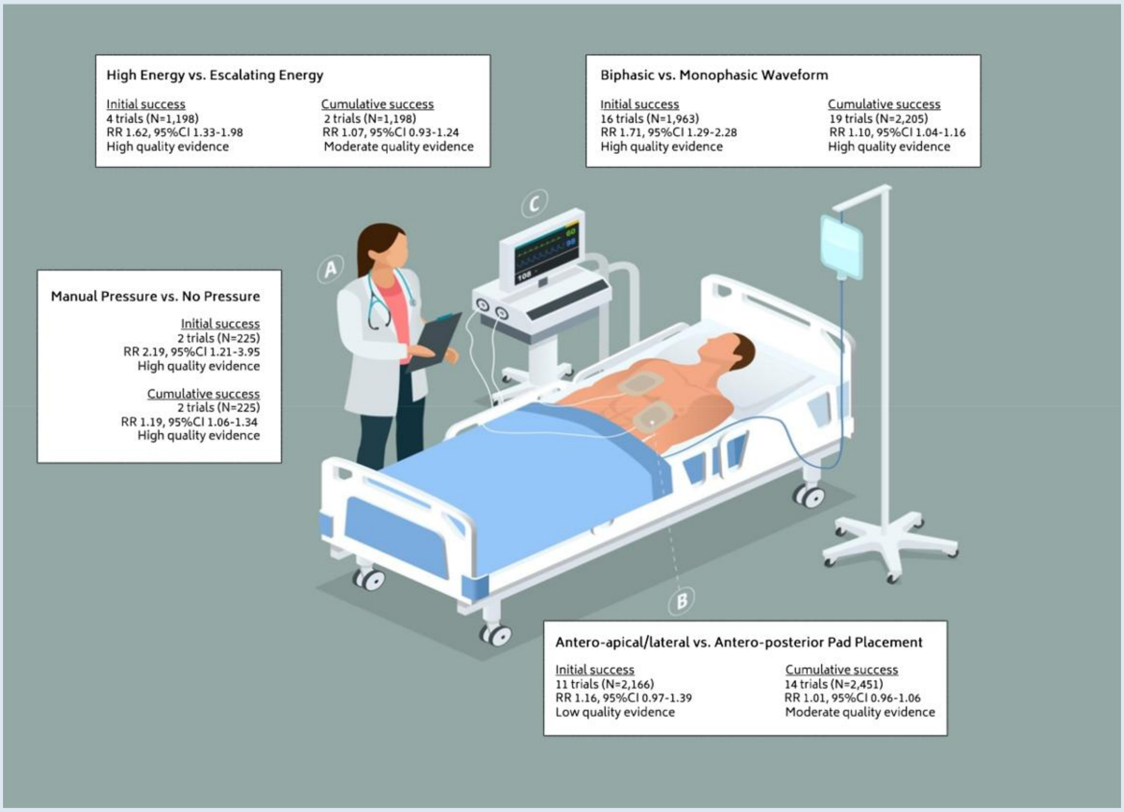
Graphical Abstract



Keywords Electrical cardioversion • Atrial fibrillation • Systematic review • Cardioversion techniques • Non-pharmacological interventions • Sinus rhythm restoration

What's new?

- Current guidelines provide limited guidance on how to perform electrical cardioversion, but our systematic review shows that clinicians can apply biphasic waveforms, high-energy (≥ 200J) shocks, and manual pressure to increase the likelihood of sinus rhythm conversion following atrial fibrillation.
- The effect of pad positioning on electrical cardioversion success is currently indeterminate. Pad placement should be studied in conjunction with two other techniques known to be effective (i.e. maximal energy and biphasic shocks) for cardioversion success.

Introduction

Atrial fibrillation (AF) is the most common arrhythmia and is associated with increased morbidity, mortality, and healthcare costs.[1–3] The prevalence and incidence of AF are increasing. An estimated 6–16 million people will have AF in the USA by 2050 and around 14 million people in Europe will have AF by 2060.[4] Electrical cardioversion is a common procedure for patients with AF to restore sinus rhythm, alleviate symptoms, and delay disease progression.[5–8] Reported acute success rates of electrical cardioversion range from 50 to 90%.[9–15] Electrical cardioversion has multiple modifiable components, including waveform phases, shock energy, pad positioning, manual pressure, and the use of adjunct medications.[14] Differences in technique may explain some of the variability in procedural success. Clinical practice guidelines provide limited guidance on how to perform electrical cardioversion.[5–8] The available evidence on interventions needs to be collated, appraised, and summarized to inform clinical practice and identify directions for future research.

This systematic review and meta-analysis aimed to compare rates of successful electrical cardioversion of AF using different techniques.

Methods

We pre-registered the protocol with Open Science Framework (DOI:10.17605/OSF.IO/FTU57).[16] We list the differences between the registered and final protocol in see Supplementary material online, *Appendix S1*.

Search strategy

We searched CENTRAL, MEDLINE, and EMBASE from inception to October 2022 and searched the grey literature.[16] An academic librarian reviewed the search strategies (see Supplementary material online, *Appendix S2*).

Eligibility criteria

We included randomized controlled trials and comparative observational studies evaluating the efficacy of a non-pharmacological intervention in patients with AF undergoing electrical cardioversion. We excluded studies where AF was induced and studies focused on atrial flutter. We did not pose restrictions on language or publication status.

Outcomes

The primary outcomes were initial and cumulative cardioversion success, defined as sinus rhythm following administration of the first and last shock, respectively. For 'cross-over' protocols, we only considered shocks delivered with the first allocated intervention. We included adverse events as secondary outcomes. We used individual studies' definitions for all outcomes.

Data collection and analysis

We selected studies using Covidence (Veritas Health Innovation, Melbourne, Australia). Two reviewers independently screened studies based on titles and abstracts. Two reviewers then independently screened full texts and recorded the main reason for exclusion. We resolved disagreements through discussion with the supervising author.

Data extraction and management

For each study, two reviewers independently collected data, resolving disagreements by discussion with the supervising author. We collected data on bibliographic information, AF duration, study protocol, anticoagulant, and anti-arrhythmic drug use, description of the intervention and comparator, electrical cardioversion success, and adverse events. We contacted authors for further information as needed.

Data synthesis and subgroup analyses

We used Review Manager 5.4 (Cochrane Collaboration) to perform meta-analysis using the Mantel–Haenszel method. Results are presented as risk ratios (RRs) with 95% confidence intervals (CI) using random-effects models. A two-sided *P*-value <0.05 was considered statistically significant. We assessed heterogeneity with the I^2 statistic and considered an I^2 value of > 50% to represent substantial heterogeneity.[17] We conducted prespecified subgroup analyses based on waveform phases, energy dose, and electrode positioning.

Assessment of the quality of evidence

We assessed risk of bias in individual studies using the Cochrane Risk of Bias 1.0 tool for randomized trials and the CLARITY tool for observational studies.[18–20] Reviewers evaluated randomized trials as having low, high, or unclear risk of bias across the domains of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias (e.g. premature study termination). We judged detection bias to be low in all studies due to the objective nature of the outcome and the short time from intervention to occurrence. We judged the risk of performance bias to be low if study protocols clearly outlined co-interventions; otherwise, we judged it to be high. We dichotomized the overall risk of bias as either low (all domains rated at a low risk of bias) or high (at least one domain rated at a high risk of bias). Reviewers assessed observational studies as having low, probably low, probably high, or high risk of bias.

We appraised the overall quality of the evidence for each comparison using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) framework.[21] Within the GRADE framework, randomized trials begin with a high-quality rating and observational studies begin with a low-quality rating. The quality of the evidence can be rated up or down based on five factors: risk of bias, directness of the evidence, heterogeneity of data, precision of results, and publication bias.

Results

Search results and study selection

Our search strategy identified a total of 15 207 unique citations, of which 258 met criteria for full-text screening. From this, 45 randomized trials (7110 participants) and 16 observational studies (4718 participants) met criteria for inclusion in the quantitative synthesis (see Supplementary material online, *Appendix S3*). Interventions studied in randomized trials included: shock waveforms (18 studies), energy dose (4 studies), pad positioning (14 studies), manual pressure (2 studies), biphasic waveform properties (5 studies), and electrode polarity (2 studies). The characteristics of the included randomized trials are summarized in *Table 1* and detailed further in Supplementary material online, *Appendix S4*. The interventions compared in the 16 observational studies included: biphasic vs. monophasic shock waveform (six studies), energy dose (two studies), pad positioning (four studies), manual pressure (two studies), and biphasic waveform properties (two studies). Supplementary material online, *Appendix S5* summarizes the characteristics of the included observational studies. Supplementary material online, *Appendix S6* summarizes the characteristics of ongoing and important excluded studies.

Assessment of risk of bias

We judged 28 trials as having an unclear risk of bias for randomization and 31 studies as having an unclear risk of bias for allocation concealment; no studies were rated high risk in these two domains. We judged all 46 trials to be at low risk of detection bias. We judged one trial to be at high risk for performance bias due to participants receiving unequal co-interventions.[45] No studies had risk of attrition or reporting bias that we judged to have an important effect on outcomes. Three trials were terminated early for benefit[44,48,63]; this is known to potentially overestimate the true effect size.[66] Supplementary material online, *Appendix S7* summarizes our judgments about each risk of bias item presented as percentages across all randomized trials. Supplementary material online, *Appendix S8* summarizes our judgements about risk of bias across included randomized trials. Supplementary material online, *Appendix S9* summarizes the risk of bias in observational studies.

Initial and cumulative cardioversion success

Table 2 summarizes the study's overall findings.

Biphasic and monophasic waveforms

Sixteen randomized trials (1963 participants) compared initial cardioversion success between biphasic and monophasic waveforms.[22–26,28,30,32–39] Biphasic waveforms resulted in an overall higher rate of cardioversion success (54 vs. 32%, RR 1.71, 95% CI 1.29–2.28, $I^2 = 85\%$, *Figure 1A*). Neither subgroup analyses comparing the two variations of the biphasic waveform (truncated exponential and rectilinear) nor subgroup analyses comparing pad positioning showed significant differences (all $P > 0.05$) (see Supplementary material online, *Appendix S10*). We judged the overall quality of evidence for initial cardioversion success to be high (see Supplementary material online, *Appendix S13*).

Nineteen randomized trials (2205 participants) compared cumulative cardioversion success between biphasic and monophasic waveforms.[22–39] Biphasic waveforms resulted in an overall higher rate of cardioversion success (93 vs. 84%, RR 1.10, 95% CI 1.04–1.16, $I^2 = 70\%$, *Figure 1B*). All trials used low-dose escalating energy shock protocols. Subgroup analyses comparing the two variations of the biphasic waveform (truncated exponential and rectilinear) did not show any significant differences ($P = 0.33$) (see Supplementary material online, *Appendix S10*). Subgroup analyses comparing pad positioning also did not show significant differences ($P = 0.32$) (see Supplementary material online, *Appendix S10*). We judged the overall quality of evidence for cumulative cardioversion success to be high (see Supplementary material online, *Appendix S13*).

Table 1 Characteristics of included studies

Author	Study arms	n	Electrode placement or waveform	Shock protocol (Joules)	Success rate (%) by attempt 1	2	3	4	5	Risk of bias
SHOCK WAVEFORM										
Ambler 2006[22]	Monophasic	68	AA	100, 200, 300, 360, 360	19	47	66	79	87	High
	Biphasic	60	AA	70, 100, 150, 200, 300	33	70	84	92	93	
Kawabata 2007[23]	MDS	77	AA	100, 200, 300, up to 360	54.6	81.8	90.9	92.2	–	Low
	BTE	77	AA	50, 100, 150, up to 175	57.1	80.5	87.0	89.6	–	
Khaykin 2003[24]	MDS	28	AP	360	–	–	21	–	–	Low
	BTE	28	AP	150, 200, 360	22	43	69	–	–	
Kirchhof 2005[25]	MDS	97	AP	50, 100, 200, 300, 360	8.3	16	48	68	80	High
	BTE	104	AP	50, 100, 200, 300, 360	25	55	82	89	95	
Kmec 2006[26]	MDS	100	AL	200, 300, 360, 360	27	60	80	83	–	Low
	BTE	100	AL	100, 120, 270, 270	50	86	93	93	–	
Kosior 2005[27]	MDS	22	AL	2 J/kg BW, then up to 2 shocks of 360 J	N/A	N/A	88	–	–	Low
	BR	26	AL	2 J/kg BW, then up to 2 shocks of 360 J	N/A	N/A	100	–	–	
Koster 2004[28]	MDS	37	AL	70, 100, 200, 360	5.4	19	38	86	–	Low
	BTE	35	AL	70, 100, 200, 360	60	80	97	97	–	
Krasteva 2001[29]	MDS	80	N/A	160	90	–	–	–	–	Low
	BTE	31	N/A	80, 100, 120, 160, 180	N/A	N/A	N/A	N/A	87	
Manegold 2007[30]	MDS	21	AP	200, 300, 360, 360	71%	N/A	N/A	95	–	Low
	BR	23	AP	100, 150, 200, 200	74%	N/A	N/A	96	–	
Marinsek 2003[31]	MDS	40	AL	100, 200, 300, 360	N/A	N/A	N/A	90	–	High
	BTE	43	AL	70, 100, 150, 200	N/A	N/A	N/A	88.3	–	
Mittal 2000[32]	MDS	77	AP	100, 200, 300, 360	21	44	68	79	–	High
	BR	88	AP	70, 120, 150, 170	68	85	91	94	–	
Neumann 2004[33]	MDS	57	AP	100, 200, 360	15.8	42.1	73.7	–	–	Low
	BTE	61	AP	100, 200, 360	57.4	95.1	100	–	–	
Page 2002[34]	MDS	107	AP	100, 150, 200, 360	22.4	43.9	53.3	85.1	–	Low
	BTE	96	AP	100, 150, 200, 360	60.4	77.1	89.6	90.6	–	
Ricard 2001[35]	MDS	27	AL	150, 360	59.3	88.9	–	–	–	Low
	BTE	30	AL	150, 360	86.7	93.3	–	–	–	
Santomauro 2004[36]	MDS	18	AP	100, 200, 300, 360, 360	5	27	50	72	78	Low
	BTE	24	AP	70, 100, 150, 200, 200	15	55	80	95	100	
Santomauro 2004[36]	MDS	18	AP	100, 200, 300, 360, 360	5	27	50	72	78	Low
	BR	22	AP	75, 100, 150, 200, 200	9	45	72	90	95	
Siaplaouras 2004[37]	MDS	108	AP	200, 300, 360, 360	67.7	N/A	N/A	96.8	–	Low
	RBW	108	AP	120, 150, 200, 200	76.4	N/A	N/A	94.3	–	
Stanaitiene 2008[38]	MDS	112	AA, AP	100, 200, 300, 360	37.5	63.4	77.7	79.5	–	High
	BTE	112	AA, AP	100, 150, 200, 300, 360	67	88.4	94.6	97.3	–	
Vaisman 2005[39]	Monophasic	22	N/A	200, 300, 360	95.5	N/A	95.5	–	–	Low
	Biphasic	21	N/A	120, 150, 200	57.1	N/A	85.5	–	–	
ENERGY DOSE										
Boodhoo 2007[40]	Escalating	125	AA-AA-AP MDS	200 AA, 360AA, 360AP	41.6	72.0	83.2	–	–	Low
	High energy	136	AA-AP-PA MDS	360AA, 360AP, 360PA	68.4	86.0	91.9	–	–	
Glover 2008[41]	Escalating	193	AA BTE	100, 150, 200, 200	47.7	76.7	87.6	90.2	–	Low
	High energy	187	AA BTE	200, 200, 200	70.6	82.9	88.2	–	–	

Continued

Table 1 Continued

Author	Study arms	n	Electrode placement or waveform	Shock protocol (Joules)	Success rate (%) by attempt					Risk of bias
					1	2	3	4	5	
[a]Gotcheva 2015[42]	Escalating	112	AL Biphasic	120, 200, 200, 360	54.5	N/A	N/A	95.5		Low
	High energy	169	AL Biphasic	200, 200, 200, 360	72.9	N/A	N/A	88.8		
Schmidt 2020[43]	Escalating	147	AP BTE	120, 150, 200	34.0	53.1	66	–	–	Low
	High energy	129	AP BTE	360, 360, 360	75.2	85.3	88.4	–	–	
PAD PLACEMENT										
Alp 2000[44]	AL	30	MDS	360	60	–	–	–	–	High
	AP	29	MDS	360	34.5	–	–	–	–	
Botto 1999[45]	AA	151	MDS	3 J/kg BW then 4 J/kg (max. 360 J)	58	76	–	–	–	High
	AP	150	MDS	3 J/kg BW then 4 J/kg (max. 360 J)	67	87	–	–	–	
Brazdzionyte 2006[46]	AL	55	BTE	100, 150, 200, 300	72.7	94.5	96.3	98.2	–	Low
	AP	48	BTE	100, 150, 200, 300	60.4	85.4	95.8	97.9	–	
Chen 2003[47]	AA	31	MDS	100, 150, 200, 300, 360	19.4	45.2	74.2	77.4	83.9	Low
	AP	39	MDS	100, 150, 200, 300, 360	23	41.0	66.7	79.5	84.6	
Kirchhof 2002[48]	AA	56	MDS	Preselected shock energies, starting at 50 J	5.4	19.7	50.1	68	78.7	High
	AP	52	MDS	Preselected shock energies, starting at 50 J	9.6	28.8	59.6	76.9	96.1	
Mathew 1999[49]	AA	45	N/A	100, 200, 300, 360	N/A	N/A	N/A	84	–	Low
	AP	45	N/A	100, 200, 300, 360	N/A	N/A	N/A	78	–	
Munoz-Martinez 2010[50]	AA	46	BTE	150, 200, 200	70	N/A	96	–	–	Low
	AP	45	BTE	150, 200, 200	40	N/A	94	–	–	
Schmidt 2021[51]	AL	233	BTE	100, 150, 200, 360	54	75	86	93	–	Low
	AP	234	BTE	100, 150, 200, 360	33	53	69	85	–	
Siaplaouras 2005[52]	AA	63	Biphasic	120, 150, 200, 200 Watts	74.6	87.3	93.6	95.2	–	Low
	AP	60	Biphasic	120, 150, 200, 200 Watts	78.3	89.9	94.9	94.9	–	
Steill 2020[53]	AL	82	Biphasic	≥ 200 (3 shocks maximum)	91.4	N/A	93.9	–	–	Low
	AP	78	Biphasic	≥ 200 (3 shocks maximum)	76.9	N/A	91.0	–	–	
Tuinenburg 1997[54]	AL	35	MDS	100, 200, 360	N/A	N/A	85.7	–	–	Low
	AP	35	MDS	100, 200, 360	N/A	N/A	82.9			
Vogiatzis 2009[55]	AA	32	MDS	200, 300, 360	43.8	62.5	96.9	–	–	Low
	AP	30	MDS	200, 300, 360	50.0	93.3	100.0	–	–	
Voskoboinik 2019[56]	AL	64	Biphasic	100, 200	N/A	76.5	–	–	–	Low
	AP	61	Biphasic	100, 200	N/A	82	–	–	–	
Walsh 2005[57]	AA	150	BTE	70, 100, 150, 200	36	66.0	82	95.3	–	Low
	AP	144	BTE	70, 100, 150, 200	31	51.4	75.7	88.2	–	
MANUAL PRESSURE OR NO PRESSURE										
Squara 2021[58]	Active compression	50	AP	50, 100, 150, 200	10	46	72	84	–	Low
	Control	50	AP	50, 100, 150, 200	34	66	86	96	–	
[b]Voskoboinik, 2019[56]	Hand-held paddles	62	AA or AP	100, 200	50	90	–	–	–	Low
	adhesive patch	63	AA or AP	100, 200	27	68	–	–	–	
BIPHASIC WAVEFORM PROPERTIES										
Alatawi 2005[59]	BTE	70	AP	50, 70, 100, 125, 150, 200, 300, 360	30	N/A	N/A	N/A	N/A	High

Continued

Table 1 ***Continued***

Author	Study arms	*n*	Electrode placement or waveform	Shock protocol (Joules)	Success rate (%) by attempt					Risk of bias
					1	2	3	4	5	
	BR	71	AP	50, 75, 100, 120, 150, 200	21	N/A	N/A	N/A	N/A	
Deakin 2012[60]	BTE	99	N/A	50, 100, 150, 200, 200	15.2	47.5	68.7	87.9	90.9	High
	BR	101	N/A	50, 100, 150, 200, 200	18.8	58.4	82.2	91.1	95.1	
Kim 2004[61]	BTE	74	AP	50, 100, 150, 200, 360	54	84	92	97	97	Low
	BR	71	AP	50, 100, 150, 200	61	79	93	97	–	
Neal 2003[62]	BTE	48	AP	50, 100, 200, 200	52.1	83.3	95.8	97.9	–	Low
	BR	53	AP	50, 100, 200, 200	64.2	94.3	100.00	100.00	–	
Schmidt 2017[63]	BTE	65	AP	100, 150, 200, 250	N/A	N/A	N/A	86	–	High
	PB	69	AP	90, 120, 150, 200	N/A	N/A	N/A	62	–	
ELECTRODE POLARITY										
Oral 1999[64]	Anterior cathodal configuration	100	MDS, AA	50, 100, 200, 300, 360	N/A	N/A	85	N/A	94	Low
	Anterior anodal configuration	100	MDS, AA	50, 100, 200, 300, 360	N/A	N/A	72	N/A	96	
Rashba 2002[65]	Anterior cathodal configuration	55	AP	50, 100, 200, 300, 360	N/A	N/A	N/A	N/A	83.4	Low
	Anterior anodal configuration	55	AP	50, 100, 200, 300, 360	N/A	N/A	N/A	N/A	78.1	

[a]Separate group involving escalating protocol based on body surface area not included.
[b]Special inclusion criterion of body mass index of 30 or greater.
Abbreviations: AA, antero-apical pad positioning; AL, antero-lateral pad positioning; AP, antero-posterior pad positioning; BR, biphasic rectilinear waveform; BTE, biphasic truncated exponential waveform; MDS, monophasic dampened sinusoidal waveform; N/A, not applicable (not reported); SR, sinus rhythm.

Energy dose

Four randomized trials (1198 participants) compared initial cardioversion success between high-energy shocks with a minimum of 200 J and shock protocols that started with low energy and escalated in the event of an unsuccessful shock.[40–43] High-energy shocks resulted in a significant improvement in overall initial cardioversion success (72 vs. 44%, RR 1.62, 95% CI 1.33–1.98, $I^2 = 72\%$, *Figure 2*). Subgroup analyses based on electrode positioning showed a significant subgroup effect for initial cardioversion success in favour of a larger effect with antero-posterior pad positioning when compared with antero-apical or antero-lateral positioning ($P = 0.003$) (see Supplementary material online, *Appendix S10*). Neither biphasic when compared with monophasic waveforms ($P = 0.93$) nor a fixed energy protocol of 200 J compared with a fixed energy protocol of 360 J ($P = 0.07$) were effect modifiers for energy dose (see Supplementary material online, *Appendix S10*). We judged the overall quality of evidence for initial cardioversion success to be high (see Supplementary material online, *Appendix S13*).

The same four trials (1198 participants) compared cumulative cardioversion success between high-energy shocks and escalating energy protocols.[40–43] High-energy shocks did not significantly improve overall cumulative cardioversion success (89 vs. 83%, RR 1.07, 95% CI 0.93–1.24, $I^2 = 91\%$, see Supplementary material online, *Appendix S10*). Subgroup analyses showed significant subgroup effects in favour of antero-posterior pad positioning ($P = 0.04$) and a fixed energy protocol using 360 J ($P = 0.04$) (see Supplementary material online, *Appendix S10*). There was no significant subgroup difference when comparing monophasic waveforms to biphasic waveforms ($P = 0.75$) (see Supplementary material online, *Appendix S10*). Quality of evidence for cumulative cardioversion success was moderate due to inconsistency (see Supplementary material online, *Appendix S13*).

Pad positioning

Eleven trials (2166 participants) compared initial cardioversion success between the antero-apical/lateral and antero-posterior pad positioning.[44–48,50–53,55,57] The overall rate of initial cardioversion success was 49% for antero-apical/lateral and 42% for antero-posterior (RR 1.16, 95% CI 0.97–1.39, $I^2 = 70\%$, *Figure 3A*). A subgroup analysis comparing trials that used biphasic waveforms (six trials, RR 1.26, 95% CI 1.04–1.53, $I^2 = 71\%$) and those that used monophasic waveforms (five trials, RR 0.96, 95% CI 0.73–1.26, $I^2 = 29\%$) did not find a significant subgroup effect ($P = 0.11$) (see Supplementary material online, *Appendix S10*). A subgroup comparison of the one trial that applied fixed, high-energy shocks (RR 1.74, 95% CI 0.97–3.11) and 10 trials that applied escalating energy shocks (RR 1.14, 95% CI 0.95–1.36, $I^2 = 71\%$) did not find a significant subgroup effect for cumulative success ($P = 0.17$) (see Supplementary material online, *Appendix S10*). Quality of evidence for initial cardioversion success was low based on inconsistency and imprecision (see Supplementary material online, *Appendix S13*).

Fourteen trials (2451 participants) compared cumulative cardioversion success between antero-apical/lateral and antero-posterior positioning.[44–53,55–57] Overall cardioversion success was 80% for the antero-apical/lateral and 77% for the antero-posterior configuration (RR 1.01, 95% CI 0.96–1.06, $I^2 = 62\%$, *Figure 3B*). A subgroup analysis comparing trials that used biphasic waveforms (seven trials, RR 1.05,

Table 2 Association of different interventions with initial and cumulative cardioversion success in patients with atrial fibrillation

Intervention	Initial success				Cumulative success			
	Events/total (no. of patients)	Effect risk ratio (95% CI)	I^2%	Quality of evidence	Events/total (no. of patients)	Effect risk ratio (95% CI)	I^2%	Quality of evidence
Shock waveform								
Monophasic	316/974	1.71 (1.29–2.28)	85	Moderate	936/1116	1.10 (1.04–1.16)	70	High
Biphasic	538/989				1016/1089			
Energy dose								
High energy	445/621	1.62 (1.33–1.98)	72	High	553/621	1.07 (0.93–1.24)	91	Low
Escalating energy	255/577				477/577			
Pad placement								
Antero-apical/lateral	540/1091	1.16 (0.97–1.39)	70	Low	984/1235	1.01 (0.96–1.06)	62	Moderate
Antero-posterior	451/1075				939/1216			
Pressure								
No pressure	22/112	2.19 (1.21–3.95)	34	High	85/112	1.19 (1.06–1.34)	9	High
Manual pressure	48/113				104/113			
Biphasic waveform properties								
Rectilinear/pulsed biphasic	111/296	1.11 (0.91–1.34)	0	Moderate	261/294	0.98 (0.89–1.08)	84	Moderate
Biphasic truncated exponential	101/291				265/286			
Polarity								
Cathodal configuration	N/A				140/155	0.99 (0.92–1.07)	15	High
Anodal configuration					139/155			

95% CI 1.00–1.10, $I^2 = 52\%$) and trials that used monophasic waveforms (seven trials, RR 0.96, 95% CI 0.87–1.05, $I^2 = 55\%$) did not find a significant subgroup effect ($P = 0.09$). A subgroup comparison of the one trial that applied fixed, high-energy shocks (RR 1.74, 95% CI 0.97–3.11) and 10 trials that applied escalating energy shocks (RR 1.01, 95% CI 0.96–1.06, $I^2 = 61\%$) did not find a significant subgroup effect for cumulative success ($P = 0.07$) (see Supplementary material online, *Appendix S10*). In the third trials that reported the average number of shocks required to cardiovert, participants randomized to antero-posterior configuration and those randomized to the antero-apical/lateral configuration converted after a mean of 2 ± 1 shocks.[46,52,55] Quality of evidence for cumulative cardioversion success was moderate due to inconsistency (see Supplementary material online, *Appendix S13*).

Manual pressure

Two trials (225 participants) compared initial cardioversion success with and without manual pressure.[56,58] One trial used paddle electrodes,[58] the other trial used manual pressure on top of adhesive electrodes.[56] One trial enrolled patients with a body mass index of 30 kg/m^2 or greater.[56] Both trials applied escalating shocks. Antero-posterior pad positioning was used in one trial and there was an equal distribution of antero-posterior and antero-apical pad positioning in the other. Manual pressure increased initial cardioversion success (42 vs. 20%, RR 2.19, 95% CI 1.21–3.95, $I^2 = 34\%$, *Figure 4A*). Quality of evidence for initial cardioversion success was high (see Supplementary material online, *Appendix S13*).

The same two trials (225 participants) compared cumulative cardioversion success with and without manual pressure.[56,58] Manual pressure application increased cumulative cardioversion success (92 vs. 76%, RR 1.19, 95% CI 1.06–1.34, $I^2 = 9\%$, *Figure 4B*). Quality of evidence for cumulative cardioversion success was high (see Supplementary material online, *Appendix S13*).

Other interventions

Nine trials (1031 participants) assessed cardioversion success with other techniques.[59,60,62–65] None of these techniques impacted initial nor cumulative cardioversion success (see Supplementary material online, *Appendix S10*). These techniques included rectilinear/pulsed biphasic compared with biphasic truncated exponential waveform (initial: four trials, RR 1.11, 95% CI 0.91–1.34, $I^2 = 0\%$; cumulative: four trials, RR 0.98, 95% CI 0.89–1.08, $I^2 = 84\%$); and anterior pad as cathode compared with anterior pad as anode (cumulative success: two trials, RR 0.99, 95% CI 0.92–1.07, $I^2 = 15\%$). Supplementary material online, *Appendix S13* summarizes the quality of evidence for these pooled estimates.

Adverse events

Reporting of adverse events varied between trials. Serious adverse events such as stroke (reported in one trial), pacemaker implantation (reported in one trial), and ventricular arrhythmia (reported in one trial) were rare (see Supplementary material online, *Appendix S11*).

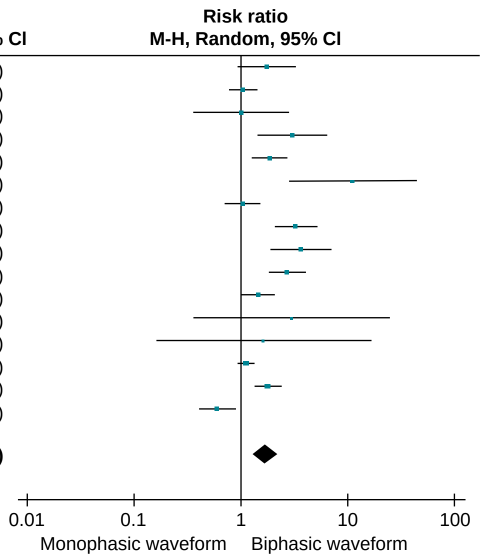
Outcomes from observational studies

Biphasic and monophasic shock waveforms were compared in six observational studies (2081 participants). When compared with monophasic waveforms, biphasic waveforms were not associated with significant differences in initial (RR 1.03, 95% CI 0.97–1.09, I^2= 68%) or cumulative (RR 1.12, 95% CI 0.97–1.29, $I^2 = 76\%$) cardioversion success. Fixed, high-energy protocols and escalating energy protocols

A Initial Cardioversion Success

Study or subgroup	Biphasic waveform Events	Biphasic waveform Total	Monophasic waveform Events	Monophasic waveform Total	Weight	Risk ratio M-H, Random, 95% CI
Ambler 2006	20	60	13	68	6.4%	1.74 (0.95, 3.20)
Kawabata 2007	44	77	42	77	8.3%	1.05 (0.79, 1.39)
Khaykin 2003	6	28	6	28	4.3%	1.00 (0.37, 2.73)
Kirchof 2005	26	104	8	97	5.6%	3.03 (1.44, 6.37)
Kmec 2006	50	100	27	100	7.8%	1.85 (1.27, 2.70)
Koster 2004	21	35	2	37	2.9%	11.10 (2.81, 43.89)
Manegold 2007	17	23	15	21	7.9%	1.03 (0.72, 1.49)
Mittal 2000	60	88	16	77	7.3%	3.28 (2.07, 5.19)
Neumann 2004	35	61	9	57	6.2%	3.63 (1.92, 6.87)
Page 2002	58	96	24	107	7.7%	2.69 (1.83, 3.97)
Ricard 2001	26	30	16	27	8.0%	1.46 (1.04, 2.06)
Santomauro 2004	4	24	1	18	1.5%	3.00 (0.37, 24.61)
Santomauro 2004	2	22	1	18	1.3%	1.64 (0.16, 16.62)
Siaplaouras 2004	82	108	73	108	8.8%	1.12 (0.95, 1.33)
Stanaitiene 2008	75	112	42	112	8.3%	1.79 (1.36, 2.34)
Vaisman 2005	12	21	21	22	7.8%	0.60 (0.41, 0.88)
Total (95% CI)		**989**		**974**	**100.0%**	**1.71 (1.29, 2.28)**
Total events	538		316			

Heterogeneity: Tau² = 0.23; Chi² = 99.97, df = 15 ($P < 0.00001$); I^2 = 85%
Test for overall effect: Z = 3.70 (P = 0.0002)



B Cumulative Cardioversion Success

Study or subgroup	Biphasic waveform Events	Biphasic waveform Total	Monophasic waveform Events	Monophasic waveform Total	Weight	Risk ratio M-H, Random, 95% CI
Ambler 2006	56	60	59	68	6.2%	1.08 (0.96, 1.21)
Kawabata 2007	69	77	71	77	6.7%	0.97 (0.88, 1.07)
Khaykin 2003	19	28	6	28	0.5%	3.17 (1.49, 6.73)
Kirchof 2005	99	104	78	97	6.5%	1.18 (1.06, 1.32)
Kmec 2006	93	100	83	100	6.6%	1.12 (1.01, 1.24)
Kosior 2005	26	26	19	22	4.5%	1.16 (0.97, 1.39)
Koster 2004	34	35	32	37	5.6%	1.12 (0.98, 1.29)
Krasteva 2001	27	31	71	80	5.2%	0.97 (0.83, 1.13)
Manegold 2007	22	23	20	21	5.8%	1.00 (0.88, 1.14)
Marinsek 2003	38	43	36	40	5.3%	0.98 (0.85, 1.14)
Mittal 2000	83	88	61	77	6.0%	1.19 (1.05, 1.35)
Neumann 2004	61	61	42	57	5.1%	1.35 (1.16, 1.58)
Page 2002	87	96	91	107	6.6%	1.07 (0.96, 1.18)
Ricard 2001	28	30	24	27	4.9%	1.05 (0.89, 1.24)
Santomauro 2004	21	22	14	12	3.0%	1.23 (0.94, 1.60)
Santomauro 2004	24	24	14	18	3.1%	1.28 (0.99, 1.66)
Siaplaouras 2004	102	108	104	108	7.7%	0.98 (0.92, 1.04)
Stanaitiene 2008	109	112	89	112	6.7%	1.22 (1.11, 1.35)
Vaisman 2005	18	21	21	22	4.1%	0.90 (0.74, 1.09)
Total (95% CI)		**1089**		**1116**	**100.0%**	**1.10 (1.04, 1.16)**
Total events	1016		936			

Heterogeneity: Tau² = 0.01; Chi² = 60.86, df = 18 ($P < 0.00001$); I^2 = 70%
Test for overall effect: Z = 3.19 (P = 0.001)

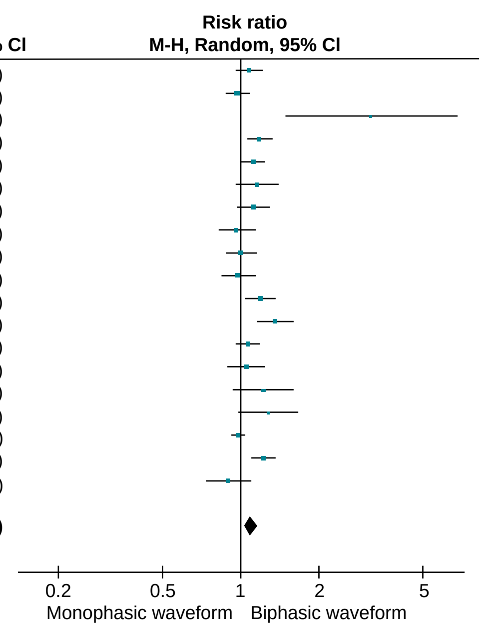


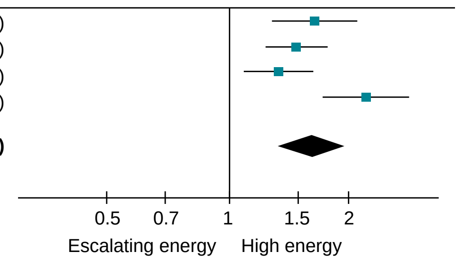
Figure 1 Forest plots for RCTs comparing biphasic and monophasic waveforms. (*A*) Initial cardioversion success. (*B*) Cumulative cardioversion success.

were compared in two observational studies (779 participants). When compared with fixed, high-energy protocols, escalating energy protocols were associated with higher rates of final cardioversion success (RR 1.06, 95% CI 1.01–1.11, $I^2 = 0\%$). Antero-apical/lateral and antero-posterior pad positioning were compared in four observational studies (533 participants). When compared with antero-posterior pads, antero-apical/lateral pads were not associated with significant differences in initial (RR 1.07, 95% CI 0.89–1.29, $I^2 = 55\%$) or cumulative cardioversion success (RR 1.04, 95% CI 0.98–1.10, $I^2 = 0\%$). Manual pressure was assessed in two observational studies (915 participants). When compared with no pressure, manual pressure was not associated with significant differences in initial cardioversion success (RR 0.78, 95% CI 0.33–1.86, $I^2 = 79\%$). However, manual pressure was associated with a higher rate of cumulative cardioversion success (RR 1.08, 95% CI 1.04–1.11, $I^2 = 4\%$). Studies that compared waveform properties found similar success with biphasic pulsed energy when compared with biphasic low energy waveform with pulsed biphasic and biphasic truncated exponential waveforms. Forest plots and data for these comparisons appear in Supplementary material online, *Appendix S12*.

A Initial cardioversion success

Study or subgroup	High energy Events	High energy Total	Escalating energy Events	Escalating energy Total	Weight	Risk ratio M-H, Random, 95% CI
Boodhoo 2007	93	136	52	125	23.4%	1.64 (1.30, 2.08)
Glover 2008	132	187	92	193	27.5%	1.48 (1.24, 1.76)
Gotcheva 2015	123	169	61	112	26.3%	1.34 (1.10, 1.62)
Schmidt 2019	97	129	50	147	22.8%	2.21 (1.73, 2.83)
Total (95% CI)		**621**		**577**	**100.0%**	**1.62 (1.33, 1.98)**
Total events	445		255			

Heterogeneity: Tau² = 0.03; Chi² = 10.82, df = 3 ($P < 0.01$); $I^2 = 72\%$
Test for overall effect: $Z = 4.73$ ($P < 0.00001$)



B Cumulative cardioversion success

Study or subgroup	High energy Events	High energy Total	Escalating energy Events	Escalating energy Total	Weight	Risk ratio M-H, Random, 95% CI
Boodhoo 2007	125	136	104	125	25.0%	1.10 (1.01, 1.21)
Glover 2008	165	187	169	193	26.0%	1.01 (0.94, 1.09)
Gotcheva 2015	149	169	107	112	26.3%	0.92 (0.86, 0.99)
Schmidt 2019	114	129	97	147	22.6%	1.31 (1.17, 1.53)
Total (95% CI)		**621**		**577**	**100.0%**	**1.07 (0.93, 1.24)**
Total events	553		477			

Heterogeneity: Tau² = 0.02; Chi² = 31.71, df = 3 ($P < 0.00001$); $I^2 = 91\%$
Test for overall effect: $Z = 0.99$ ($P = 0.32$)

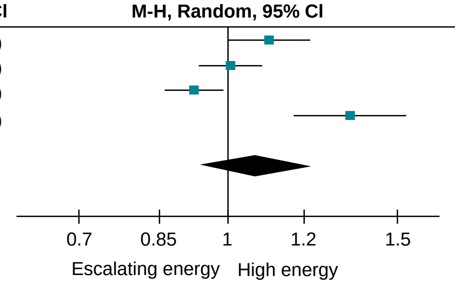


Figure 2 Forest plots of RCTs comparing fixed, high energy and low-dose, escalating energy. (*A*) Initial cardioversion success. (*B*) Cumulative cardioversion success.

Discussion

This systematic review and meta-analysis of randomized trials and observational studies identified three techniques that improve cardioversion success for patients with AF. Biphasic shock waveforms nearly doubled initial cardioversion success and increased cumulative success by about 10%. High-energy shocks using at least 200 J increased initial success by approximately 60%. Biphasic, high-energy shocks can increase efficacy and minimize the number of shocks needed for restoration of sinus rhythm. Manual pressure, which was studied primarily in obese patients, resulted in a two-fold increase in success and may be considered in these patients. The optimal electrode position remains unclear. No randomized trial has compared antero-posterior and antero-apical/lateral pad configurations while using biphasic, high-energy shocks.

Biphasic waveforms result in higher initial and cumulative shock success; we rated this evidence as high quality. These findings were consistent when tested across subgroups of biphasic waveform properties and pad position. The superiority of biphasic waveforms is hypothesized to stem from their ability to compensate for transthoracic impedance.[32]

Fixed, high-energy shocks result in higher initial cardioversion success; we rated this evidence as high quality. Escalating-energy protocols increase until reaching high energy; and as expected, have similar cumulative success as high-energy protocols. Observational series have suggested that this effect may be even more pronounced in patients with longer AF durations.[67] Experimental studies on animals have suggested that lower energy settings may reduce skin burns, patient discomfort, and myocardial damage.[68] However, such adverse events are rare in clinical practice.[40–43] In contrast, minimizing the number of shocks is desirable because it requires less sedation, shortens the overall procedure time, and minimizes patient discomfort.[14]

Manual pressure with handheld paddles or active compression increases the efficacy of both initial and cumulative cardioversion; we rated this evidence as high quality. These interventions are hypothesized to lower thoracic impedance.[69] Although we judged this evidence as high-quality based on the GRADE framework, it has limitations. These studies included only 225 patients, and one study was limited to obese patients.[56,58] Clinicians may consider manual pressure using gloved hands on the first attempt in obese patients and during repeated attempts in others.

We found no difference in cardioversion success when comparing antero-posterior to antero-apical/lateral pad position. We rated this evidence as low quality for initial cardioversion success and moderate quality for cumulative success. Importantly, evidence for pad position is limited because it has not been studied in conjunction with the other two techniques known to be effective (i.e. maximal energy and biphasic shocks). Biological arguments support both configurations of pad placement. Antero-posterior placement may result in a more direct shock vector to the atria, resulting in reduced transthoracic impedance, except in patients with larger chests.[57,70,71] In contrast, antero-apical/lateral pads may capture more myocardial cells overall.[72] Because the effect could differ based on patient anatomy, clinicians may consider the opposite configuration when the first fails.

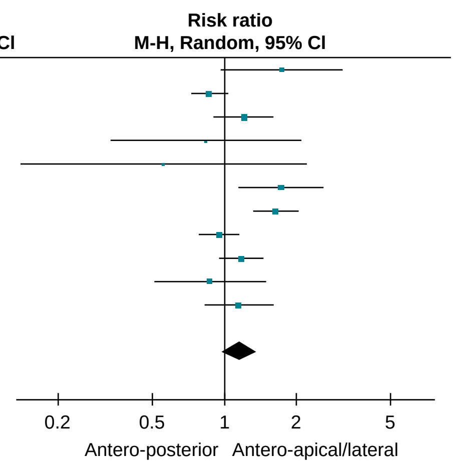
This review found no significant differences between the biphasic waveform subtypes or differing electrode polarity. These interventions seem unlikely to impact cardioversion success.

Clinical practice guidelines make a number of statements related to cardioversion techniques, but these have not been based on systematic reviews.[5–8,73] The 2014 American Heart Association/American College of Cardiology Guidelines discuss high energy, biphasic waveforms, changing shock vectors, and applying pressure to improve energy delivery, but do not make practice recommendations.[8,73] The 2020

A Initial cardioversion success

Study or subgroup	Antero-apical/lateral Events	Antero-apical/lateral Total	Antero-posterior Events	Antero-posterior Total	Weight	Risk ratio M-H, Random, 95% CI
Alp 2000	18	30	10	29	5.9%	1.74 [0.97, 3.11]
Botto 1999	88	151	101	150	13.7%	0.87 [0.73, 1.03]
Brazdzionyte 2006	40	55	29	48	11.3%	1.20 [0.91, 1.59]
Chen 2003	6	31	9	39	3.0%	0.84 [0.33, 2.10]
Kirchhof 2002	3	56	5	52	1.5%	0.56 [0.14, 2.22]
Munoz-Martinez 2010	32	46	18	45	8.7%	1.74 [1.16, 2.61]
Schmidt 2021	126	233	77	234	12.8%	1.64 [1.32, 2.04]
Siaplaouras 2005	47	63	47	60	13.3%	0.95 [0.78, 1.16]
Stiell 2020	112	244	95	244	13.0%	1.18 [0.96, 1.45]
Vogiatzis 2009	14	32	15	30	6.5%	0.88 [0.51, 1.49]
Walsh 2005	54	150	45	144	10.4%	1.15 [0.83, 1.59]
Total (95% CI)		**1091**		**1075**	**100.0%**	**1.16 [0.97, 1.39]**
Total events	540		451			

Heterogeneity: Tau² = 0.05; Chi² = 33.41, df = 10 (P = 0.0002); I^2 = 70%
Test for overall effect: Z = 1.68 (P = 0.09)



B Cumulative cardioversion success

Study or subgroup	Antero-apical/lateral Events	Antero-apical/lateral Total	Antero-posterior Events	Antero-posterior Total	Weight	Risk ratio M-H, Random, 95% CI
Alp 2000	18	30	10	29	0.7%	1.74 [0.97, 3.11]
Botto 1999	115	151	131	150	8.8%	0.87 [0.78, 0.97]
Brazdzionyte 2006	54	55	47	48	12.3%	1.00 [0.95, 1.06]
Chen 2003	26	31	33	39	4.4%	0.99 [0.81, 1.22]
Kirchhof 2002	44	56	50	52	6.6%	0.82 [0.71, 0.95]
Mathew 1999	38	45	35	45	4.5%	1.09 [0.89, 1.33]
Munoz-Martinez 2010	41	46	32	45	4.2%	1.25 [1.01, 1.55]
Schmidt 2021	216	233	200	234	11.7%	1.08 [1.02, 1.16]
Siaplaouras 2005	60	63	57	60	10.6%	1.00 [0.93, 1.09]
Stiell 2020	119	244	108	244	4.8%	1.10 [0.91, 1.33]
Tuinenburg 1997	30	35	29	35	4.5%	1.03 [0.84, 1.27]
Vogiatzis 2009	31	32	30	30	10.2%	0.97 [0.89, 1.06]
Voskoboinik 2019	49	64	50	61	5.2%	0.93 [0.78, 1.12]
Walsh 2005	143	150	127	144	11.4%	1.08 [1.01, 1.16]
Total (95% CI)		**1235**		**1216**	**100.0%**	**1.01 [0.96, 1.06]**
Total events	984		939			

Heterogeneity: Tau² = 0.00; Chi² = 34.49, df = 13 (P = 0.001); I^2 = 62%
Test for overall effect: Z = 0.38 (P = 0.70)

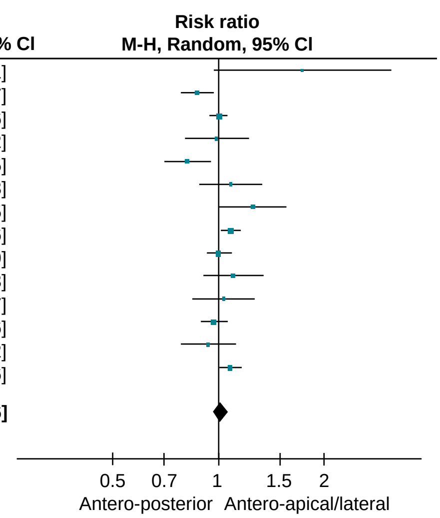


Figure 3 Forest plots for RCTs comparing antero-apical/lateral and antero-posterior pad placement. (*A*) Initial cardioversion success. (*B*) Cumulative cardioversion success.

Canadian Cardiovascular Society Guidelines recommend (strong recommendation; low-quality evidence) at least a 150 J biphasic waveform for electrical cardioversion.[5] These guidelines discuss that pad positioning does not seem to impact efficacy and that manual pressure may facilitate cardioversion in obese patients. The 2020 European Society of Cardiology Guidelines discuss the superiority of biphasic waveforms, but do not make a practice recommendation.[7] These guidelines also discuss that anterior–posterior pads are more effective, but offer the caveat that some studies have shown no difference. A practical guidance document that was published by the European Heart Rhythm Association in 2020 states that antero-posterior pad placement is more effective than antero-apical.[6] The evidence provided by this systematic review will inform practice recommendations.

Strengths

This is the first systematic review to comprehensively summarize and appraise the evidence on techniques impacting cardioversion success.[6,14,74–76] Our protocol was preregistered and our review assessed the methodological quality of individual studies. We used the GRADE approach to assess the quality of evidence. We performed subgroup analyses to assess interventions in the context of other co-interventions.

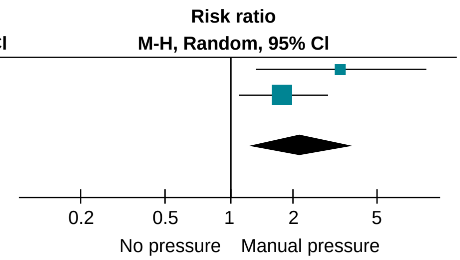
Limitations

The limitations of this review are inherent to the included studies. The main limitation was the heterogeneous combinations of interventions used in different studies. Although we attempted to assess this using subgroup analyses, these findings should be considered exploratory. Pre-treatment with anti-arrhythmic drugs also varied; it is established to improve acute and long-term success of cardioversion.[15] Although included studies did not provide data on long-term maintenance of sinus rhythm, it seems unlikely that these interventions would affect this outcome. Finally, adverse effects were not consistently reported or were not specified across studies.

A Initial cardioversion success

Study or subgroup	Manual pressure Events	Manual pressure Total	No pressure Events	No pressure Total	Weight	Risk ratio M-H, Random, 95% CI
Squara 2021	17	50	5	50	31.1%	3.40 [1.36, 8.50]
Voskoboinik 2019	31	63	17	62	68.9%	1.79 [1.11, 2.89]
Total (95% CI)		**113**		**112**	**100.0%**	**2.19 [1.21, 3.95]**
Total events	48		22			

Heterogeneity: Tau² = 0.07; Chi² = 1.52, df = 1 (P = 0.22); I^2 = 34%
Test for overall effect: Z = 2.60 (P = 0.009)



B Cumulative cardioversion success

Study or subgroup	Manual pressure Events	Manual pressure Total	No pressure Events	No pressure Total	Weight	Risk ratio M-H, Random, 95% CI
Squara 2021	48	50	42	50	64.8%	1.14 [1.00, 1.31]
Voskoboinik 2019	56	63	43	62	35.2%	1.28 [1.06, 1.55]
Total (95% CI)		**113**		**112**	**100.0%**	**1.19 [1.06, 1.34]**
Total events	104		85			

Heterogeneity: Tau² = 0.00; Chi² = 1.10, df = 1 (P = 0.29); I^2 = 9%
Test for overall effect: P = 2.96 (P = 0.003)

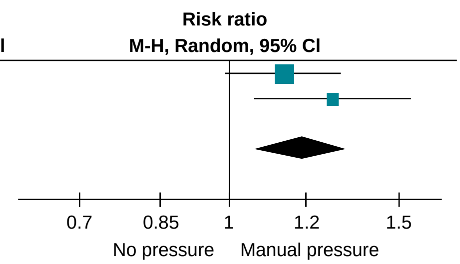


Figure 4 Forest plots for RCTs comparing manual pressure and no manual pressure. (*A*) Initial cardioversion success. (*B*) Cumulative cardioversion success.

Conclusions

Biphasic shock waveforms, high-energy shocks, and manual pressure using paddle electrodes or applied on top of adhesive electrodes increase the efficacy of cardioversion of AF. Other interventions, particularly pad placement, require further study. Considering the variability in AF cardioversion success, these findings will help guide future research.

Supplementary material

Supplementary material is available at *Europace* online.

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IMAGES IN ELECTROPHYSIOLOGY

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Selective sparing of Purkinje fibres with pulsed-field myocardial ablation

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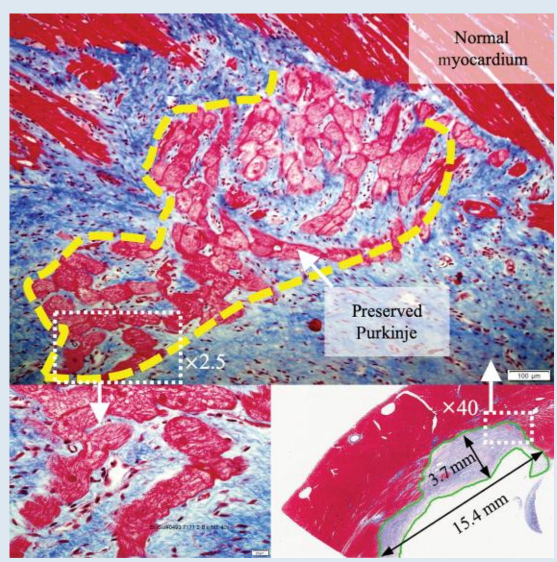
The effect of pulsed fields on the conduction system has not been well characterized. Selected lesions ($n = 26$) from four swine ventricles were submitted as part of a dosing study after bipolar, biphasic ablation using a multielectrode catheter (Faraflex, Farapulse Inc.) that delivers, microsecond pulses (2.2 kV)—four applications/site were applied. Histology after 4 weeks revealed a single image of viable Purkinje fibres (PjF), despite the ablation of adjacent cardiomyocytes as evidenced by fibrosis surrounding the PjF (*Panel*). The sparing of PjF seen, although a solitary finding, in this study may suggest a lower susceptibility than cardiomyocytes and requires further confirmatory studies.



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Conflict of interest: V.Y.R. hold stock options in Farapulse, Inc. J.S.K. serves as a consultant to Farapulse. The other authors report no conflicts.