Appendix C1

Supplement Post ROSC Angiography

Summary of observational data with high risk of bias and very low certainty of evidence.

POST ROSC no STEMI and all rhythms

For the critical outcome of survival to hospital discharge we identified very-low certainty evidence from 1 observational studies (Kim 2018) reporting adjusted odds ratios. which showed no benefit from the use of early coronary angiography when compared to late/no angiography [OR 1.60 (95% CI 0.73 to 3.53)].

For the critical outcome of survival to hospital discharge we identified very-low certainty evidence from 5 observational studies (Hanuschak 2019; Kern 2015; Kim 2018; Kleissner 2015; Vadeboncoer 2018) reporting unadjusted odds ratios. One study (Kleissner 2015) found no effect of early coronary angiography compared to late/no coronary angiography with OR 1.80 (95% CI 0,37 to 8.82). One study found a decrease in survival (Kim 2018) [OR 0.41 (95% CI 0.23 to 0.72)] and 3 studies found increased survival with early coronary angiography (Hanuschak 2019; Kern 2015; Vadeboncoer 2018). The effect sizes ranged from a low of OR 2.80 (95% CI 1.94 to 4.04) to a high of OR 7.42 (95% CI 5.44 to 10.12).

For the critical outcome of ***survival at 30 days***, we identified very-low certainty from one study (Bro-Jeppesen 2012) which found no effect of early coronary angiography compared to late/no angiography [ORadj 1.42 (95% CI 1.00 to 2.50) and ORunadj 1.66 (95% CI 0.96 to 2.88).

For the critical outcome of ***survival at 3-6 months***, we identified very-low-certainty evidence from 1 observational studies (Kleissner 2015) with unadjusted effect estimates of OR 1.48 (95% CI 0.55 to 3.99).

For the critical outcome of ***survival at 1-3 years***, we identified very-low-certainty evidence from 1 observational study (Bro-Jeppesen 2012) which found no effect of early coronary angiography compared to late/no angiography with an adjusted OR 0.97 (95% CI 0.76 to 1.25).

We identified very-low-certainty evidence from 2 observational studies (Bro-Jeppesen 2012; Dankiewicz 2015). One study (Bro-Jeppesen 2012) found increased survival with early coronary angiography [OR 1.92 (95% CI 1.11 to 3.32)] and one study (Dankiewicz 2015) found no effect [OR 1.27 (95% CI 0.91 to 1.79)].

For the critical outcome of survival with ***favourable neurologic outcome at hospital discharge***, we identified very-low-certainty evidence from 1 observational study (Bro-Jeppesen 2012) with adjusted effect estimates which found no effect of early coronary angiography compared to late/no angiography [OR 1.50 (95% CI 0.80 to 2.90).

We identified very-low-certainty evidence from 3 observational studies (Bro-Jeppesen 2012; Hanuschak 2019; Kleissner 2015) with unadjusted effect estimates. One study (Kleissner 2015) found on effect with early coronary angiography [OR 1.28 (95% CI 0.51 to 3.20)]. Two studies (Bro-Jeppesen 2012; Hanuschuk 2019) found increased survival with favourable neurologic outcome with early coronary angiography with a range of effect estimates from a low of OR 1.94 (95% CI 1.19 to 3.17) to a high of OR 8.37 (95% CI 6.18 to 11.35).

For the critical outcome of survival with ***favourable neurologic outcome at 30 days***, we identified very-low-certainty evidence from 1 study (Kim 2018) with adjusted effect size which found no effect with early coronary angiography with an OR 1.92 (95% CI 0.95 to 3.85)

We identified very-low-certainty evidence from 2 observational studies (Kim 2018; Kern 2015) with unadjusted effect estimates. One study (Kern 2015) found an increase in survival with favourable neurologic outcome at 30 days with early coronary angiography [OR 2.77 (95% CI 1.92 to 4.00)] and one study (Kim 2018) found a decrease with early coronary angiography [OR 0.45 (95% CI 0.26 to 0.77)].

For the critical outcome of survival with ***favourable neurologic outcome at 3-6 months***, we identified very-low-certainty evidence from one observational study (Dankiewicz 2015) with adjusted effect estimate which found no effect of early coronary angiography OR 0.92 (95% CI 0.69 to 1.18).

We identified very-low certainty evidence from 2 studies (Dankiewicz 2015; Kleissner 2015) with unadjusted effect estimates. Both studies (Dankiewicz 2015; Kleissner 2015) found no benefit with early coronary angiography [OR 1.36 (95% CI 0.97 to 1.91) and OR 2.01 (95% CI 0.77 to 5.24) respectively].

Table 1: Studies examining post-ROSC coronary angiography in patients with no ST elevation on ECG and all ECG rhythms

Survival								
	Adjusted				Unadjusted			
Author	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival
Bro-Jeppesen 2012		1.42 (1.00, 2.50)				1.66 (0.96, 2.88)		1.92 (1.11, 3.32)
Dankiewicz 2015				0.97 (0.76, 1.25)				1.27 (0.91, 1.79)
Hanuschak 2019					7.42 (5.44, 10.12)			
Kern 2015					2.80 (1.94, 4.04)			
Kim 2018	1.60 (0.73, 3.53)				0.41 (0.23, 0.72)			
Kleissner 2015					1.80 (0.37, 8.82)		1.48 (0.55, 3.99)	
Vadeboncoer 2018					3.26 (2.51, 4.23)			
Favourable Neurologic Outcome								
	Adjusted				Unadjusted			
Author	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival

Bro-Jeppesen 2012	1.50 (0.80, 2.90)				1.98 (1.14, 3.43)			
Dankiewicz 2015			0.92 (0.69, 1.18)				1.36 (0.97, 1.91)	
Hanuschak 2019					8.37 (6.18, 11.35)			
Kern 2015						2.77 (1.92, 4.00)		
Kim 2018		1.92 (0.95, 3.85)				0.45 (0.26, 0.77)		
Kleissner 2015					1.28 (0.51, 3.20)		2.01 (0.77, 5.25)	

POST ROSC no STEMI and shockable initial rhythm

For the critical outcome of ***survival to hospital discharge*** we identified very-low certainty evidence from two observational studies (Garcia 2016; Hollenbeck 2014) which reported adjusted effect estimates for early coronary angiography compared to late/no angiography. One studies (Hollenbeck 2014) identified benefit from early angiography [OR 2.86 (95% CI 1.43 to 5.56)]. A single study (Garcia 2016) found no effect of early angiography [OR 1.73 (95% CI 0.80 to 3.74)].

We also identified very-low certainty evidence from two studies (Garcia 2016; Hollenbeck 2014) reporting unadjusted effect estimates for early coronary angiography compared to late/no angiography. One study (Hollenbeck 2014) identified benefit with early angiography with an OR 2.04 (95% CI 1.24 to 3.34). Garcia (2016) found no benefit with early coronary angiography [OR 1.25 (95% CI 0.67 to 2.34)].

For the critical outcome of ***survival at 30 days*** we identified very-low certainty evidence from one study (Elfwen 2018) which reported an adjusted effect estimate of OR 1.42 (95% CI 1.00 to 2.02).

We also identified very-low certainty evidence from one study (Elfwen 2018) reporting unadjusted effect estimates with an OR 1.73 (95% CI 1.28 to 2.34).

For the critical outcome of ***survival at 1-3 years*** we identified very-low certainty evidence from a single study (Elfwen 2018) which reported adjusted effect estimates and found benefit with early angiography with an OR 1.35 (95% CI 1.04 to 1.77).

We identified very-low certainty evidence from 2 studies (Elfwen 2018; Hollenbeck 2014) which reported unadjusted effect estimates. Both studies found benefit with early angiography with effect estimates ranging from a low of OR 1.77 (95% CI 1.32 to 2.39) to a high of OR 3.48 (95% CI 2.36 to 5.14).

For the critical outcome of ***favourable neurologic outcome at hospital discharge*** we identified very-low certainty evidence from one observational studies (Garcia 2016) identifying benefit with the use of early angiography compared to late/no angiography with an adjusted OR 2.77 (95% CI 1.31 to 5.85).

We also identified very-low certainty evidence from two observational studies (Garcia 2016; Hollenbeck 2014) which reported unadjusted effect estimates for early coronary angiography compared to late/no angiography. One study (Hollenbck 2014) found benefit with early coronary angiography [OR 1.94 (95 %CI 1.19 to 3.17). The other study (Garcia 2016) found no benefit with early coronary angiography [OR 1.70 (95% CI 0.95 to 3.06)].

For the critical outcome of survival with ***favourable neurologic outcome at 1-3 years*** we identified very-low certainty evidence from 1 study (Hollenbeck 2014) reporting unadjusted effect estimates with an OR 2.11 (95% CI 1.30 to 3.45).

Table 2: Studies examining post-ROSC coronary angiography in patients with no ST elevation on ECG and initial shockable rhythms

Survival								
	Adjusted				**Unadjusted**			
Author	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival
Garcia 2016	1.73 (0.80, 3.74)				1.25 (0.67, 2.34)			
Elfwen 2018		1.42 (1.00, 2.02)		1.35 (1.04, 1.77)		1.73 (1.28, 2.34)		1.77 (1.32, 2.39)
Hollenbeck 2014	2.86 (1.43, 5.56)				2.04 (1.24, 3.34)			2.06 (1.26, 3.35)
Favourable Neurologic Outcome								
	Adjusted				**Unadjusted**			
Author	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival
Garcia 2016	2.77 (1.31, 5.85)				1.70 (0.95, 3.06)			
Hollenbeck 2014					1.94 (1.19, 3.17)			2.11 (1.30, 3.45)

POST ROSC With ST-segment elevation on ECG

For the critical outcome of ***survival at hospital discharge*** we identified very-low certainty evidence from one study (Garcia 2016) which reported adjusted effect estimates for early coronary angiography compared to late/no coronary angiography for patients with ROSC after out-of-hospital cardiac arrest. The study found no effect with early angiography [OR 1.89 (95% CI 0.48 to 7.40)].

We also identified very-low certainty evidence from 4 studies (Garcia 2016; Hanuschack 2019; Kern 2015; Pleskot 2008) which reported unadjusted effect estimates for early coronary angiography compared to late/no angiography. Two studies (Hanuschak 2019; Pleskot 2008) identified benefit from early angiography with OR 4.07 (95% CI 2.85 to 5.82) and OR 11.67 (95% CI 1.11 to 122.38) respectively. Two other studies (Garcia 2016; Kern 2015) found no benefit with early angiography with OR 1.65 (95% CI 0.45 to 6.09) and OR 0.85 (95% CI 0.31 to 2.32).

For the critical outcome of ***survival at 1-3 years*** we identified very-low certainty evidence from one study (Pleskot 2008) which reported unadjusted effect estimates with an OR 11.67 (95% CI 1.11 to 122.38).

For the critical outcome of survival with ***favourable neurologic outcome at hospital discharge***, we identified very-low-certainty evidence from 2 observational study (Garcia 2016; Weiser 2013) with adjusted effect estimates which found no difference in favourable neurologic outcome with early coronary angiography with an OR 1.12 (95% CI 0.30 to 4.19) and OR 1.17 (95% CI 0.45 to 3.04) respectively.

We also identified very-low certainty evidence from 4 studies (Garcia 2016; Hanuschack 2019; Pleskot 2008; Weiseer 2013) which reported unadjusted effect estimates for early coronary angiography compared to late/no angiography. Two studies (Hanuschak 2019; Weiser 2013) identified benefit from early angiography with OR 4.05 (95% CI 2.82 to 5.83) and OR 1.94 (95% CI 1.05 to 3.59) respectively. Two other studies (Garcia 2016; Pleskot 2008) found no benefit with early angiography with OR 1.03 (95% CI 0.28 to 3.76) and OR 7.50 (95% CI 0.73 to 76.77).

For the critical outcome of ***survival at 1-3 years*** we identified very-low certainty evidence from one study (Pleskot 2008) which reported unadjusted effect estimates with an OR 11.67 (95% CI 1.11 to 122.38).

Table 3: Studies examining post-ROSC coronary angiography in patients with ST elevation on ECG

Survival								
	Adjusted				Unadjusted			
Author	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival
Garcia 2016	1.89 (0.48, 7.40)				1.65 (0.45, 6.09)			
Hanuschak 2019					4.07 (2.85, 5.82)			
Kern 2015					0.85 (0.31, 2.32)			
Pleskot 2008					11.67 (1.11, 122.38)			11.67 (1.11, 122.38)
Favourable Neurologic Outcome								
	Adjusted				Unadjusted			
Author	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival
Garcia 2016	1.12 (0.30, 4.19)				1.03 (0.28, 3.76)			

Hanuschak 2019					4.05 (2.82, 5.83)			
Pleskot 2008					7.50 (0.73, 76.77)			11.67 (1.11, 122.38)
Weiser 2013	1.17 (0.45, 3.04)				1.94 (1.05, 3.59)			

POST ROSC all ECGs (undifferentiated) all initial rhythms

For the critical outcome of ***survival to hospital discharge*** we identified very-low certainty evidence from four studies (Bougouin 2018; Shin 2017; Stub 2011; Zanuttini 2012) which reported adjusted effect estimates for early coronary angiography compared to late/no coronary angiography. Two studies (Shin 2017; Zanuttini 2012) identified benefit with early angiography with effect estimates of OR 2.70 (95% CI 1.60 to 4.60) and OR 2.32 (95% CI 1.23 to 4.38). Two studies (Bougouin 2018; Stub 2011) found no benefit with early angiography [OR 1.20 (95% CI 0.80 to 1.90) to OR 4.30 (95% CI 0.97 to 19.00)].

We also identified very-low certainty evidence from 21 studies (Study Citations) which reported unadjusted effect estimates for early angiography compared to late/no angiography in patients with ROSC after out-of-hospital cardiac arrest. Seventeen studies (Study Citations) identified benefit of early coronary angiography with unadjusted effect estimates ranging from a low of OR 1.73 (95% CI 1.34 to 2.23) to a high of OR 7.60 (95% CI 3.20 to 17.50). Four studies (Study Citations) found no benefit with the use of early angiography with effect estimates ranging from a low of OR 1.20 (95% CI 0.50 to 2.90) to a high of OR 2.46 (95% CI 1.00 to 6.04).

For the critical outcome of ***survival at 30-days*** we identified very-low certainty evidence from three studies (Casella 2014; Jaeger 2018; Waldo 2013) reporting adjusted effect estimates for the use of early coronary angiography compared to late/no angiography in patients with ROSC after out-of-hospital cardiac arrest. All three studies (Casella 2015; Jaeger 2018; Waldo 2013) identified benefit with the use of early angiography with adjusted effect estimates ranging from a low of OR 1.52 (95% CI 1.33 to 1.72) to a high of OR 2.38 (1.06, 5.26).

We identified very-low certainty evidence from four observational studies (Bro-Jeppesen 2012; Casella 2015; Jaeger 2018; Winther-Jensen 2018) reporting unadjusted effect estimates for early coronary angiography compared to late/no angiography for patients with ROSC after out-of-hospital cardiac arrest. All four studies (Bro-Jeppesen 2012; Casella 2015; Jaeger 2018; Winther-Jensen 2018) identified benefit with early angiography with effect estimates ranging from a low of OR 1.61 (95% CI 1.05 to 2.47) to a high of OR 2.59 (95% CI 1.24 to 5.43).

For the critical outcome of ***survival at 1-3 years*** we identified very-low certainty evidence from one observational studies (Casella 2015) reporting adjusted effect estimates for early coronary angiography compared to late/no angiography which showed benefit with early coronary angiography with an OR 3.57 (95% CI 1.32 to 10.00).

We also identified very-low certainty evidence from four studies (Bergman 2016; Bro-Jeppesen 2012; Casella 2015; Geri 2015) which reported unadjusted effect estimates for early coronary angiography compared to late/no angiography. All four studies (Bergman 2016; Bro-Jeppesen 2012; Casella 2015; Geri 2015) identified benefit with early angiography with effect estimates ranging from a low of OR 1.84 (95% CI 1.20 to 2.81) to a high of OR 4.51 (95% CI 2.07 to 9.87).

For the critical outcome of survival with ***favourable neurologic outcome at hospital discharge***, we identified very-low-certainty evidence from five observational study (Bougouin 2017; Casella 2015; May 2020; Reynolds 2014; Shin 2017) with adjusted effect estimates. All five studies found improved outcomes with early coronary angiography with effect estimates ranging from a low of OR 1.43 (95% CI 1.02 to 2.00) to a high of OR 36.36 (95% CI 2.13 to 631.14).

We identified very-low-certainty evidence from 11 observational studies (Bro-Jeppesen 2012; Callaway 2014; Casella 2015; Chelvanathan 2016; Hanuschak 2019; Jentzer 2018; Mooney 2011; Reynolds 2014; Shin 2017; Tomte 2011; Vadeboncoer 2018) with unadjusted effect estimates. All 11 studies found benefit with early coronary angiography with effect estimates ranging from a low of OR 1.83 (95% CI 1.20 to 2.80) to a high of OR 10.54 (95% CI 6.68 to 16.62).

For the critical outcome of survival with ***favourable neurologic outcome at 3-6 months*** we identified very-low certainty evidence from one observational study (Nielsen 2009) which identified improved outcome with early coronary angiography compared to late/no coronary angiography with a reported unadjusted OR 3.11 (95% CI, 2.40 to 4.04).

Table 4: Studies examining post-ROSC coronary angiography in patients without ST elevation on ECG and any initial rhythm

Survival								
	Adjusted				Unadjusted			
Author	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival
Aurore 2010					2.74 (1.57, 4.76)			
Bergman 2016					2.50 (1.70, 3.67)			3.48 (2.36, 5.14)
Bougouin 2018	1.20 (0.80, 1.90)				3.92 (2.89, 5.34)			
Bougouin 2017								
Bro-Jeppesen 2012						1.61 (1.05, 2.47)		1.84 (1.20, 2.81)
Callaway 2014					4.93 (4.17, 5.83)			
Casella 2015		2.38 (1.06, 5.26)		3.57 (1.32, 10.00)		2.59 (1.24, 5.43)		4.51 (2.07, 9.87)
Chelvanathan 2016					3.81 (1.96, 7.38)			
Geri 2015					2.40 (1.91, 3.02)			2.88 (2.19, 3.79)
Hanuschak 2019					5.12 (4.29, 6.10)			

Jaeger 2018		1.52 (1.33, 1.72)				2.56 (2.32, 2.83)		
Jentzer 2018					2.85 (2.04, 3.99)			
Kern 2015					2.49 (1.85, 3.35)			
Kroupa 2017					1.20 (0.50, 2.90)			
Lam 2018					3.00 (1.69, 5.28)			
Mooney 2011					2.65 (1.24, 5.67)			
Nadar 2018					2.12 (0.69, 6.49)			
Nielsen 2009					1.73 (1.34, 2.23)			
Reynolds 2014					2.26 (1.70, 3.01)			
Shin 2017	2.70 (1.60, 4.60)				6.80 (4.49, 10.28)			
Stub 2011	4.30 (0.97, 19.00)				7.60 (3.20, 17.50)			
Vadeboncoer 2018					2.31 (1.90, 2.79)			
Waldo 2013		2.29 (1.19, 4.41)			2.46 (1.00, 6.04)			
Wijesekera 2014					4.41 (1.36, 14.32)			
Winther-Jensen 2018						1.74 (1.11, 2.63)		
Zanuttini 2012	2.32 (1.23, 4.38)				1.74 (0.77, 3.97)			
Functional Neurologic Outcome								
	Adjusted				Unadjusted			
Author	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 year Survival

Bougouin 2017	1.43 (1.02, 2.00)							
Bro-Jeppesen 2012					1.83 (1.20, 2.80)			
Callaway 2014					5.20 (4.40, 6.15)			
Casella 2015	36.36 (2.13, 631.1)				5.42 (2.28, 12.86)			
Chelvanathan 2016					9.41 (4.19, 21.15)			
Hanuschak 2019					5.66 (4.74, 6.77)			
Jentzer 2018					3.16 (2.05, 4.89)			
May 2020	1.45 (1.02, 2.09)							
Mooney 2011					3.29 (1.50, 7.24)			
Nielsen 2009							3.11 (2.40, 4.04)	
Reynolds 2014	1.92 (1.20, 3.07)				3.32 (2.47, 4.47)			
Shin 2017	2.30 (1.60, 3.10)				10.54 (6.68, 16.62)			
Tomte 2011					2.45 (1.04, 5.74)			
Vadeboncoer 2018					4.19 (3.45, 5.08)			

POST ROSC all ECGs (undifferentiated) initial shockable rhythm

For the critical outcome of ***survival at hospital discharge*** we identified very-low certainty evidence from 3 studies (Aissaoui 2018; Bergman 2016; Garcia 2016) reporting adjusted effect estimates comparing early coronary angiography to late/no coronary angiography in comatose post-cardiac arrest patients. Two studies (Aissaoui 2018; Bergman 2016) found benefit with early coronary angiography with effect estimates of OR 7.01 (95% CI 4.80 to 10.23) and OR 2.86 (95% CI 1.43 to 5.56) respectively. A single study (Garcia 2016) found no benefit with an OR 1.60 (95% CI 0.83 to 3.08).

We also identified very-low certainty evidence from 5 studies (Bergman 2016; Cronier 2014; Garcia 2016; Nanjayya 2012; Strote 2012) reporting unadjusted effect estimates. Four studies (Bergman 2016; Cronier 2014; Garcia 2016; Strote 2012) found benefit with early coronary angiography with effect estimates ranging from a low of OR 2.50 (95% CI 1.70 to 3.67) to a high of OR 3.41 (95% CI 1.20 to 9.67). A single study (Nanjayya 2012) found no benefit with an OR 2.03 (95% CI 0.78 to 5.31).

For the critical outcome of ***survival at 30-days*** we identified very-low certainty evidence from a single study (Jaeger 2018) comparing early coronary angiography to late/no coronary angiography which reported adjusted effect estimates which found improved survival with early coronary angiography [OR 1.74 (95% CI 1.37 to 2.21)].

For the critical outcome of ***survival at 1-3 years*** we identified very-low certainty evidence from a single study (Bergman 2016) reporting unadjusted effect estimates for early coronary angiography compared to late/no coronary angiography which found improved survival with early coronary angiography [OR 3.48 (95% CI 2.36 to 5.14)].

For the critical outcome of ***favourable neurologic outcome at hospital discharge*** we identified very-low certainty evidence from 2 studies (Aissaoui 2018; Garcia 2016) which reported adjusted effect estimates for early coronary angiography compared to late/no coronary angiography for comatose post-cardiac arrest patients. Both studies found improved outcome with early coronary angiography with effect estimates of OR 6.40 (95% CI 3.90 to 10.50) and OR 1.99 (95% CI 1.07 to 3.72) respectively.

We also identified very-low certainty evidence from four studies (Garcia 2016; Nanjayya 2012; Strote 2012; Vyas 2015) which reported unadjusted effect estimates for early coronary angiography compared to late/no coronary angiography. Two studies (Strote 2012; Vyas 2015) found improved outcome with early coronary angiography with effect estimates of OR 2.16 (95% CI 1.20 to 3.89) and OR 2.29 (95% CI 2.01 to 2.60) respectively. Two studies (Garcia 2016; Nanjayya 2012) found no benefit with early coronary angiography with effect estimates of OR 1.45 (95% CI 0.54 to 3.89) and OR 1.56 (95% CI 0.94 to 2.56) respectively.

For the critical outcome of ***favourable neurologic outcome at 30 days*** we identified very-low certainty evidence from a single study (Jaeger 2018) which reported adjusted effect estimates for early coronary angiography compared to late/no coronary angiography for comatose post-cardiac arrest patients which found improved outcome with early coronary angiography [OR 1.57 (95% CI 1.23 to 2.01)].

Table 5: Studies examining post-ROSC coronary angiography in patients with undifferentiated ECG and initial shockable rhythm

Survival								
	Adjusted				Unadjusted			
Author	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival
Aissaoui 2018	7.01 (4.80,10.23)							
Bergman 2016	2.86 (1.43, 5.56)				2.50 (1.70, 3.67)			3.48 (2.36, 5.14)

Cronier 2014					3.41 (1.20, 9.67)			
Garcia 2016	1.60 (0.83, 3.08)				1.31 (0.77, 2.27)			
Jaeger 2018		1.74 (1.37, 2.21)						
Nanjayya 2012					2.03 (0.78, 5.31)			
Strote 2012					2.74 (1.46, 5.15)			
Favourable Neurologic Outcome								
	Adjusted				Unadjusted			
Author	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival	Hospital Discharge	30-Day Survival	3-6 Month Survival	1-3 Year Survival
Aissaoui 2018	6.40 (3.90, 10.50)							
Garcia 2016	1.99 (1.07, 3.72)				1.56 (0.94, 2.56)			
Jaeger 2018		1.57 (1.23, 2.01)						
Nanjayya 2012					1.45 (0.54, 3.89)			
Strote 2012					2.16 (1.20, 3.89)			
Vyas 2015					2.29 (2.01, 2.60)			

Appendix C2

Table 1. Characteristics of included studies

Author/Year	Patient Number	Country	Study duration	Patient aracteristics	Design	Outcomes	STEMI and no STEMI	STEMI	No STEMI	All rhythms	Shockable	Non shockable
RCTS												
Lemkes 2019	552	Netherlands	2015-2018	Included: OHCA Initial shockable rhythm Unconscious after ROSC Excluded Signs of STEMI on ECG in the ED Shock Obvious non- coronary cause of the arrest.	RCT	Survival at 90 days, Survival to HD, FNO at 90 days, PCI/CABG rates, recurrent VT or VF requiring defibrillation, bleeding, acute renal failure, renal replacement therapy, shock	-	-	+	-	+	-
Elfwen 2019	79	Sweden	2015 - 2017	Included: Witnessed OHCA; Age> 18 years ROSC; admitted alive to hospital Without ST-segment elevation or new LBBB Excluded: Obvious non-cardiac causes Life expectancy < one year Expected time to CAG >120 min Known pregnancy Patients not unconscious (GCS>8)	RCT	Survival at 24 h, subarachnoid haemorrhage, recurrent VT/VF, bleeding, bradyarrhythmias needing pacing	-	-	+	+	-	-
Observational studies												
Aissaoui 2018	1502	France, SDEC registry	2011-2015	Included: • OHCA • age ≥18 years • initial shockable rhythm • admitted alive to hospital • no obvious extra-cardiac cause • no prior terminal condition	Retrospective	Survival to HD, FNO at 1 month	+	-	-	-	+	-
Aurore 2010	445	France	2000-2006	Included: • ROSC after OHCA	Retrospective	Survival to HD	+	-	-	+	-	-

Bergman 2016	456	Netherlands	2003-2010	Included: • >18 years • admitted after OHCA • known initial rhythm	Retrospective	Survival to HD 1 and 5 years, FNO at HD	+	-	-	+	+	+
Bougouin 2018	1817	France, SDEC registry	2011-2015	Included: • age≥ 18 years • admitted with ROSC • OHCA . Excluded • prior terminal condition • obvious noncardiac cause	Retrospective	FNO at HD	+	-	-	+	-	-
Bougouin 2017	1410	France, PROCAT registry, single centre	2000-2013	Included • OHCA • age>18 years • admitted in an ICU with ROSC after CA	Retrospective	Survival to HD, FNO at HD	+	-	-	+	-	-
Bro-Jepessen 2012	360	Denmark, Single centre	2004 - 2010	Included • ≥18 years • admitted with sustained ROSC • OHCA Excluded • GCS ≥9 • cardiogenic shock upon admission	Prospective	Survival to HD and at 1 year, FNO at HD, Successful PCI	+	-	+	+	-	-
Callaway 2014	3981	USA, Canada, Multicentre	2007-2009	Included: • age > 18 years • OHCA delivered to hospital with a pulse or regained a pulse in the ED • survived for >60 min after hospital arrival • EMS-witnessed cardiac arrest • patients with tracheostomies Excluded: • prisoners • pregnant women • patients with “DNR” directives • patients with blunt, penetrating or burn-related trauma • cardiac arrest due to exsanguination	Retrospective	Survival to HD, FNO at HD, Stroke/ICH, recurrent arrest, sepsis, pneumonia, bleeding	+	-	-	+	-	-
Casella 2015	141	Italy, Single centre	2004 - 2012	Included: • ≥18 years of age • no obvious extra-cardiac aetiology • admitted alive to hospital after OHCA Excluded: • GCS ≥9 upon admission • terminal illness	Prospective	Survival at 30 days or at discharge survival at 1 year, FNO at HD, sepsis, bleeding	+	-	-	+	-	-

Chelvanathan 2016	176	Canada, Single centre			Retrospective	Survival to HD, FNO at HD	+	-	-	+	-	-
Cronier 2011	111	France, Multicentre	2003-2008	Included: • Age ≥ 18 • ROSC following OHCA • shockable rhythm	Prospective	Survival to HD	+	-	-	-	+	-
Dankiewicz 2015	544	Multiple Countries; Europe, Australia, Multicentre	2010 - 2013	Included: • OHCA of presumed cardiac cause • no STEMI	Post-hoc analysis of RCT	Survival at the end of the study, FNO at 6 months, complications, Successful PCI, bleeding	-	-	+	+	-	-
Elfwen 2018	799	Sweden, Different national registers, multicentre	2008 - 2013	Included: • bystander-witnessed OHCA • age> 18 years • shockable first rhythm • admitted alive to hospital Excluded: • GCS >8 • age >80 years	Retrospective	Survival at 30 days and at 1 and 3 years	-	-	+	-	+	-
Garcia 2016	315	USA, CARES registry	2013-2014	Included: • Prehospital CA • age >18 and <76 years • arrest of presumed cardiac etiology	Retrospective	Survival to HD, FNO at HD	+	+	+	-	+	-
Geri 2015	1722	France, Multicentre	2000-2013	Included: • Nontraumatic OHCA	Retrospective	Survival to 30 days, Survival to a median follow up 3.2 years	+	-	-	+	-	-
Hanuschak 2019	2578	Canada, Multicentre	2010-2014	Included: • age>17 years • treated by EMS • OHCA • alive six hours following ED arrival Excluded: • pre-existing DNR order • obvious non-cardiac issue	Retrospective	Survival to HD, FNO at HD	+	+	+	+	-	-
Hollenbeck 2014	269	USA, INTCAR registry	2005-2011	Included: • age ≥18 years • survived to hospitalization • comatose state • cardiac arrest due to VT or VF Excluded: • patients with ECG criteria for STEMI	Retrospective	Survival to HD, Survival to a mean follow up 5.7 to 6 months; FNO at HD, FNO to a mean follow up 5.7 to 6 months	-	-	+	-	+	-

Jaeger 2018	4046	France, REAC registry	2011-2016	Included: • age >18 years • cardiac cause • transported to the hospital	Retrospective	Survival at 30 days, FNO at 30 days	+	-	-	+	+	+
Jentzer 2018	599	USA, Multicentre	2005-2013	Included: • OHCA of presumed cardiac etiology Excluded: • Subjects who died or failed to achieve ROSC in the ED • patients receiving ongoing resuscitation at the time of CAG	Prospective	Survival to HD, FNO at HD, complications, Successful PCI, bleeding	+	-	-	-	-	-
Kern 2015	745	USA, INTCAR registry	2006-2011	Included: • patients ≥18 years • survived to hospitalization in a comatose state after cardiac arrest	Retrospective	Survival to HD, FNO at 6.5 ±4.5 months	+	+	+	+	-	-
Kim 2019	227	Korea, Multicentre	2010-2015	Included: • adult (>18 years) • non-traumatic OHCA survivors • treated with TTM	Retrospective	Survival at 30 days, FNO at 30 days	-	-	+	+	-	-
Kleisner 2015	99	Czech Republic, Single centre	2007-2014	Included: • OHCA survivors who were admitted to ICU Excluded: • Patients with acute STEMI or myocardial infarction with left bundle branch block	Prospective	Survival at discharge and at 6 months, FNO at discharge and at 6 months	-	-	+	+	-	-
Kroupa 2017	102	Czech Republic, Single centre	2011 - 2013	Included: • age>18 years • OHCA • admitted to the CCU	Retrospective	Survival to HD, Survival at 1 year	+	-	-	+	-	-
Lam 2018	323	USA, Single centre	2007-2014	Included: • patients with OHCA • who achieved ROSC • admitted to hospital Excluded: • angiography at an acute care hospital prior to transfer • incomplete medical records	Retrospective	Survival to HD	+	-	-	+	-	-
May 2020	966	USA, Multicentre	2006 - 2017	Included: • Unconscious patients (GCS <6) • age≥18 years • admitted to the intensive care unit • ROSC after OHCA • presumed cardiac etiology	Retrospective	Survival to HD FNO at HD and at 6 months	+	-	-	+	-	-

Mooney 2011	140	USA, Single centre	2006-2009	Included: • OHCA • unresponsive after ROSC • collapse to ROSC <60 minutes Excluded: • comatose before arrest • active bleeding • do-not-resuscitate directives	Prospective	Survival to HD, FNO at 6.5 ±4.5 months	+	-	-	+	-	-
Nadar 2018	216	Oman, Single centre	2012 - 2016	Included: • individuals > 18 years • OHCA Excluded: • clear non cardiac cause of CA • dead on arrival to hospital • chronicle terminal illness	Retrospective	Survival to HD	+	-	-	+	-	-
Nanjayya 2012	70	Australia, Single centre	2003 - 2008	Included: • age≥18 years • successful ROSC • VF/pVT OHCA • admitted to ICU	Retrospective	Survival to HD, FNO at HD	+	-	-	-	+	-
Nielsen 2009	986	USA, Europe, Multicentre	2004-2008	Included: • ROSC after CA • treated in ICU • GCS<8	Prospective	Survival to HD, Survival at 6-12 months, FNO to hD, FNO at 6-12 months	+	-	-	+	-	-
Plescot 2008	26	Czech Republic, Multicentre	2002-2004	Included: • ROSC • OHCA • admitted to hospital Excluded: • cardiac arrest in the presence of EMS • terminal illness • non-cardiac etiology of CA	Prospective	Survival to HD and at 1 year, FNO at HD and at 1 year	-	+	-	+	-	-
Reynolds 2014	1011	USA, Single centre	2005-2012	Included: • ≥ 18 years • ROSC • OHCA, IHCA Excluded: • traumatic or surgical causes of arrest • immediate re-arrest and failure to resuscitate • withdrawal of care within 6 h of return of pulses because of advanced directives or wishes	Retrospective	Survival to HD, FNO to HD	+	-	-	+	-	-

Shin 2017	607	Korea, Captures registry	2014-2014	Included: • OHCA • without a definite non-cardiac cause of arrest Excluded: • no ROSC • age <18 years • not transferred by EMS • incomplete data	Prospective	Survival to HD, FNO to HD	+	-	-	+	-	-
Strote 2012	240	USA, Multicentre	1999 - 2002	Included: • ROSC from OHCA • VF or VT as the first identified rhythm	Retrospective	Survival to HD, FNO to HD	+	-	-	-	+	-
Stub 2011	125	Australia, Single centre	2002-2003 (control) 2007-2009	Included: • OHCA • VF • sustained ROSC >20 min • admitted to hospital	Retrospective	Survival to HD	+	-	-	+	-	-
Tomte 2011	174	Norway, Multicentre	2003 – 2009	Included: • OHCA • presumed cardiac origin • surviving to ICU admission Excluded: • initially treated at other hospitals	Prospective	FNO to HD	+	-	-	+	-	-
Vadenbocoer 2018	1881	USA, CARES registry	2010-2014	Included: • age ≥18 years • OHCA • transported initially or transferred to a Cardiac Receiving Centre Excluded: • prehospital resuscitation not initiated • cause of CA presumed to be non-cardiac • patient with a DNR order • the patient died in the ED	Prospective	Survival to HD, FNO to HD	+	-	+	+	-	-

Vyas 2015	4029	USA, CARES registry	2010-2013	Included: • age ≥18 years • OHCA • VF/ VT or unknown shockable rhythm • sustained ROSC ≥20 min • admission to hospital Excluded: • patients with no report data on performance of CAG • hospitals that did not perform CAG on any cardiac arrest patient and were also confirmed to not have a cardiac catheterization laboratory • missing data on the date of CAG or survival	Retrospective	Survival to HD, FNO to HD	+	-	-	-	+	-
Waldo 2013	110	USA, ACTIVATE SF registry	2008-2012	Included: • cardiac arrest successfully resus-citated.	Retrospective	Survival to hospital discharge and at 30 days	+	-	-	+	-	-
Weiser 2013	249	Austria, Single centre	2005-2010	Included: • Survivors of OHCA • cardiac aetiology with good neurological performance • age ≥18 years • ST-segment elevation in their first ECG after sustained ROSC	Prospective	Survival at 30 days, FNO at 30 days	-	+	-	+	-	-
Wijesekera 2014	78	Australia, Single centre	2007-2009	Included: • OHCA • age ≥18 years • admitted to either the coronary or the intensive care unit	Retrospective	Survival to HD, FNO to HD	+	-	-	+	-	-
Winther - Jensen	704	Denmark, Multiple centre	2007–2011	Included: • age⩾18 years • OHCA • presumed cardiac aetiology • successful resuscitation or ongoing CPR at hospital arrival • dispatch by the physician-based EMS	Retrospective	Survival at 30 days	+	-	-	+	-	-

Zanuttini 2012	93	Italy, Single centre	2008 - 2011	Included: • OHCA • age >18 years • sustained ROSC (≥120 minutes) • persistent unconscious state at hospital admission • absence of any obvious extracardiac cause	Retrospective	Survival to HD	+	-	-	+	-	-

HD: hospital Discharge, FNO: Favorable Neurologic Outcome, ROSC: Return of Spontaneous Circulation, OHCA: Out of Hospital Cardiac Arrest, GCS: Glasgow Coma Scale, ED: Emergency Department, DNR : Do Not Resuscitate, ICH: intracranial haemorrhage, SPARC: Post Arrest Resuscitation Care , EMS: emergency medical services, CAG: coronary angiography

Appendix C3

Cryotherapy for Epistaxis: Experimental Study Characteristics and Findings

Author, year, country	Study design	Population	Intervention	Control	Outcome	Findings on our outcomes, as presented in article.
Ozturk, 2014, Turkey	Observation	15 patients (mean age=28.8; 9 female) least 18 years with no nasal symptoms within 3 weeks, and not pregnant.	Nasal dorsal skin cooling using two ice applied to left (L) and right (R) side of nose for 10 minutes (n=15).	No application, baseline	Cross-sectional area (cm2) and nasal cavity volume (cm3) via acoustic rhinometry	* Mean values for sum of the L and R first minimal cross-sectional area and second minimal cross-sectional area revealed no statistical differences, for either parameter at any between any intervals. * Means values for nasal cavity volume revealed no statistical differences, for any parameter, between any intervals.
Porter, 1991, United Kingdom	Cross-over, Randomized	16 healthy subjects (mean age=32, range 25-40) with no history of nasal disease, previous nasal surgery or symptoms and a normal rheoscopic examination.	Ice contained with a surgical glove applied to forehead or mouth for 3 minutes each (n=16).	Same, but at body temperature for 3 minutes each.	Nasal mucosal blood flow, measured in flux (velocity and concentration of the moving blood cells)	* Oral ice packs produced a significant decrease in nasal mucosal blood flow ($p<0.05$, average decrease=23% [standard error=5.9]) compared to control (average decrease=5%; standard error not calculated). * Oral ice packs produced a fall in flux in 9 of 16 (56%) subjects, a rise in 1 (6%), and 6 (37%) experienced no change. * Ice packs to forehead produced a fall in flux in 1 of 16 (6%) subjects, a rise in 1 (6%).
Porter, 1991b United Kingdom	Cross-over, Randomized	13 healthy subjects (mean age=30, range 25-40) with no nasal disease or treatment.	a. Ice pack wrapped in paper toweling held to the forehead by subject for 15 minutes. b. Ice cubes sucked in the mouth for 15 minutes.	No application, baseline	Nasal submucosal temperature (°C)	* A significant difference between the nasal submucosal temperature ice pack to forehead (a) compared to ice cubs in mouth (b) (p=.0.026), favoring ice cubes alone. * A significant difference between nasal submucosal temperature in ice pack to forehead compared to combined stimulus (c) (p=.0.006), favoring combined stimulus.

			c. combination of (a) and (b) for 15 minutes.			*In all subjects (n=13, 100%) ice cubes in mouth (b) produced a lower nasal submucosal temperature. The ice pack to the forehead (a) produced a decrease in nasal mucosal temperature in 7 of 13 (53%) subjects.
Scheibe, 2006, Germany	Cross-over	15 healthy subjects (range 25-40, 7 female) with no reported breathing difficulties, acute nasal allergies, or an acute rhinitis; nasal endoscopy by an ENT specialist revealed no pathology.	Ice collar (4°C) placed onto neck region for 10 minutes.	No application, baseline	Nasal blood volume via optical rhinometry (measured in nm) for whole nose and at septum, randomized.	*A significant (p<0.01) decrease in blood volume could be seen for regional measurements at the septum. * Decrease in nasal blood volume at the nasal septum was, on average, observed after approximately 2 minutes t_1=111 sec ± 73 sec); decrease reached its maximum after approximately 6 minutes ($t_{2=}$337 sec ± 119 sec).
Teymoortash, 2003, Germany	Cross-over	56 healthy subjects (mean age=30, range 17-48) with normal rhinoscopy and no history of nasal allergy or acute or recurrent symptoms of rhinitis.	Ice pack applied all-round the neck for 5 minutes.	No application, baseline	Nasal mucosal microcirculatory blood flow via laser Doppler flowmetry, nasal mucosal blood content (indirectly via conventional computer-aided anterior rhinomanometer by measuring alternations in nasal airflow and airway patency).	* After cold application, nasal mucosal blood flow decreased from 1368.8 ± 927.9 to 1130.5 ± 792.2). Difference between before and after cold application was not significant (P=0.11). * Total nasal inspiratory airflow before application was 513.9±190.4 cm^3/s, and after exposure to cold 471.5±164.6 cm^3/s (P=0.08). * Total nasal expiratory airflow before application was 474.2±211.7 cm^3/s and after exposure to cold 443.1±162.4 cm^3/s (P=0.30)
Yamagiwa, 1990, Denmark	Cross-over	10 healthy subjects (mean age=21±11.0, range 24-54) with no significant complaints or rhinoscopically overt nasal abnormalities.	Feet cooling (both) in large tub (0-4°C) immersed 30 cm from heel for 5 minutes, (n=10). One hand and forearm cooling in bucket (0-4°C)	No application, baseline	Nasal cavity volume (mL) rhinometry for L and R cavities.	* Foot cooling arm. In the exposure period, nasal airway volume was significantly higher than preexposure values in 4 of 10 (40%) of subjects, none showed significantly lower values. * Hand cooling arm. In the exposure period, nasal airway volume was significantly higher than preexposure values in 1 of 9 (11%) of subjects, lower in

immersed to around 23 cm from the middle fingertip for 5 minutes (n=9).

2 of 9 (22%), and no difference in 6 of 9 (66%)

Appendix C4

Cryotherapy for Epistaxis: Gray literature study characteristics and findings

Author, year, country	Study design, setting/audience	Intervention Concepts	Cryotherapy Statements	Direct Pressure Application Time
Pope, 2005, UK {Pope 2005 309}	Narrative: Clinical practice	Direct pressure Patient position Cryotherapy	"...improved by a cold compress or the patient sucking on ice." p.310	NA
Wong, 2018, Australia {Wong 2018 E13}	Narrative: Family practice	Direct pressure Patient position Cryotherapy	"Applying ice packs around the neck and having the patient suck on ice significantly reduces nasal mucosa blood flow and can slow down the bleeding.7" p.E16	10 min
Record, 2015, United States {Record 2015 484}	Practice guideline: Nursing	Direct pressure Patient position Cryotherapy	"Ice compresses to the forehead or neck may be used, but studies are inconclusive as to the usefulness of this maneuver (Teymoortash 2003; Scheibe, 2006)." p.487	10 min
Upile, 2008, United Kingdom {Upile 2008 1349}	Protocol: United Kingdom Healthcare System, first aid	Direct pressure Cryotherapy	"…pinching the whole of the cartilaginous tip of the nose for 30 min followed by another 30 min of pressure and pack of ice on bridge of nose if bleeding continued."	30 min + 30 min
O'Sullivan, 2020, Ireland {O'Sullivan 2020}	Informational: Website	Direct pressure Cryotherapy	"…putting an ice pack on to their forehead."	20 min
Beck, 2018, German [Beck 2018 12}	Review: primary and secondary care	Direct pressure Patient position Cryotherapy	"Local application of ice, e.g., at the back of the neck, is intended to encourage vasoconstriction of the blood vessels of the nose." Its therapeutic value is a matter of debate and has been challenged in the literature (38)."	15-20