

S1 File - Wever et al. 2015 - Determinants of the efficacy of cardiac ischemic preconditioning: a systematic review and meta-analysis of animal studies

Text A - Detailed Methods

This systematic review is based on published results of animal experiments studying the effects of local or remote IPC on MI, which we identified using a systematic, computerized search in MEDLINE (via PubMed) and EMBASE. The inclusion criteria and method of analysis were pre-specified and documented in an *a priori* protocol (see <http://www.dcn.ed.ac.uk/camarades/>). This review is reported according to the PRISMA guidelines.

1.1 Amendments to the systematic review protocol

We extracted data on three additional study quality indicators, to obtain a comprehensive overview of study quality, and to allow for better comparison with systematic reviews in other fields of research. The additional items were: reporting of a conflict of interest statement (Y/N), reporting of ethical approval of the experiment (Y/N) and reporting of regulation of body temperature within a physiological range during surgery (Y/N). We did not perform meta-analysis on these items.

We omitted the planned subgroup analysis of total risk of bias score due to the poor reporting of many of the risk of bias items, since we expect this would severely hamper the analysis and would likely produce unreliable results.

1.2 Literature search strategy, inclusion and exclusion criteria

The full search strategies for PubMed and EMBASE are included in the supplemental material, and involved the search components “animal”^{1,2}, “heart”, “ischemia reperfusion injury” and “preconditioning”. We searched the databases for published articles up to January 2nd 2014. No language or date restrictions were applied. If necessary, papers in languages other than English were translated by scientists (native speakers for that particular language) within the Radboud university medical center or the University of Edinburgh.

We included studies in the systematic review if they fulfilled all of the following criteria: 1) the study assessed the effect of IPC on myocardial infarction and reported the mean and variance of the infarct size as a percentage of the area at risk (IS/AAR%), as well as the number of animals that these figures were based on; 2) the study was performed in animals *in vivo*; 3) the study was an original full paper which presented unique data. We excluded studies if 1) experiments were performed only in genetically modified animals; 2) animals underwent any co-intervention other than sham IPC or administration of vehicle.

We used Early Review Organizing Software (EROS; Institute of Clinical Effectiveness and Health Policy, Buenos Aires, Argentina) to randomly allocate each reference to two independent reviewers, who screened it for inclusion on the basis of title and abstract. In case of doubt, the whole publication was evaluated. Two independent reviewers subsequently assessed full-text copies of all publications eligible for inclusion and included them if they met our prespecified inclusion criteria. Disagreements were solved by discussion.

1.3 Study characteristics and data extraction

In each publication, we identified all independent comparisons of the infarct size in IPC-treated animals *versus* controls. We extracted data on study design, including the animals used (species, strain, sex, age, weight, and the presence of comorbidities or other conditions), the myocardial infarction model (pre-operative opioid use, anesthetic agent used during surgery, class of anesthetic agent used, site of coronary occlusion, duration of index ischemia and timing of the outcome measure) and the IPC intervention (site of IPC, remote organ, duration of ischemic stimulus, duration of intermittent reperfusion periods, the number of cycles, and interval between IPC and myocardial index ischemia; see supplemental figure SF1). We also recorded bibliographic details such as author, journal, language and year of publication.

We extracted data on infarct size if raw data or group averages, standard deviation (SD) or standard error (SE) and number of animals per group (n) were reported, or could be recalculated. If two or more identical comparisons existed (e.g. two separate experiments, with the same control and experimental groups), they were analyzed separately. In case of missing outcome measure data, we attempted to contact authors for additional information. If the data could not be obtained, we used a conservative estimate if possible. In case the group size was reported as a range (e.g. 6-9) in combination with an SD, we used the lowest number of animals in our meta-analysis. In case the SE was reported, we used the highest number of animals to recalculate the most conservative estimate of the SD. If no conservative estimate could be made we excluded the comparison from the analysis. If data were presented only graphically, we measured them using digital image analysis software (ImageJ; <http://rsbweb.nih.gov/ij/>). If multiple experimental groups were compared to the same control group, we corrected the group size of the control group for the number of comparisons made (n/number of comparisons).

1.4 Data handling exceptions

For two comparisons (both from³) for which the number of IPC cycles was reported to be 12 or more, we used 12 as the number of cycles in our analysis.

For five comparisons (one each from⁴⁻⁸), the duration of the ischemic period of the IPC stimulus differed between cycles. We therefore used the average duration of an ischemic period (total ischemic time/# cycles) in our analysis. The same approach was used for four comparisons in which the duration of the intermittent reperfusion periods differed between cycles (one each from^{7, 9-11})

For studies investigating "repeated IPC", i.e. applying an interval of one or several days between IPC stimuli, we used the duration of the intermittent reperfusion periods within one IPC stimulus as the intermittent reperfusion duration in our analysis (e.g. comparisons from^{3, 10, 12-20}). *N.B.* in such cases, the number of IPC cycles used is the total of all IPC cycles in the entire protocol.

One study⁸ states that the variance of their data are reported as SD, but are in the SE range. In our meta-analysis, entering these data as SD resulted in an enormous deviation of the study data in terms of variance and weight. We attempted to clarify this issue by contacting the authors, but received no response. We therefore treated the data conservatively and assumed that they were in fact reported as SE.

1.5 Assessment of methodological quality

We used the SYRCLE Risk of Bias tool²¹ to assess the risk of bias in the included studies. Two independent reviewers assessed each publication and disagreements were solved by discussion. Concerning the number of excluded animals, we assumed that there had been no exclusion if the number of animals per group mentioned in the materials and methods section was identical to the number stated in the results section or figure legends. In addition, we extracted data on reporting of any measure of randomization and any measure of blinding, in order to distinguish between reporting of measures to report bias and actual risk of bias. We assessed reporting of a sample size calculation an additional study quality indicator.

1.6 Data synthesis and statistical analyses

Data were analyzed using STATA SE, version 11.2 (StataCorp, College Station, TX, USA). All data were extracted in the same unit of analysis (IS/AAR%). For each independent comparison, we calculated an effect size as a raw difference in means (MD; the mean of the experimental group minus the mean of the control group) of IS/AAR% and corresponding 95% confidence interval (CI). To account for anticipated heterogeneity, we pooled effect sizes using random effect meta-analysis, which takes into account the precision of individual studies and the variation between studies and weights each study accordingly. Heterogeneity was quantified using I^2 and T^2 statistics (see²² for meta-analysis details).

We performed pre-specified subgroup analyses, using meta-regression, to explore sources of heterogeneity and assess the impact methodological and study quality indicators on the observed efficacy of IPC. Covariates assessed were: species, sex, comorbidity, opioid use pre-IPC, site of IPC, number of IPC cycles, duration of one ischemic cycle of IPC, total duration of IPC ischemia and duration of the delay between IPC and IR. For total duration of IPC ischemia, comparisons were stratified using increments (with increasing orders of magnitude) of $\log_{10}(0.4)$ minutes. For IPC to IR delay, comparisons were stratified using increments of $\log_{10}(0.8)$ minutes. The percentage of between-study variance explained by variables of interest was assessed using the T^2 and adjusted R^2 statistic.

We adjusted our significance level using the Holm-Bonferroni method²³ ($1-(1-\alpha)^{1/m}$) to account for multiple comparisons.

We assessed for potential publication bias by visually inspection for asymmetry in funnel plots, performing Duval and Tweedie's trim and fill analysis²⁴ and Egger's regression analysis²⁵ for small study effects.

1.7 Sensitivity analyses

To assess the robustness of our findings, sensitivity analysis was performed for the cut-off points for the subgroups of total IPC ischemia and IPC to IR delay. For total IPC ischemia, the increment between categories was changed from $\log_{10}(0.4)$ minutes to $\log_{10}(0.3)$ or $\log_{10}(0.5)$ minutes. For IPC to IR delay, the increment between categories was changed from $\log_{10}(0.8)$ minutes to $\log_{10}(0.7)$ or $\log_{10}(0.9)$ minutes.

Thirteen publications (²⁶⁻³⁸) reported data from a myocardial infarction model in which a coronary-to-carotid artery shunt was used for cardiac reperfusion. We decided to consider this procedure part of the infarction model, rather than a co-intervention, but investigated the effect of our decision by excluding these studies in a sensitivity analysis.

Post-hoc, we tested the robustness of our findings using the MD by re-running our analysis using the standardized difference in means (SMD).

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Text B - Full search strategies

Pubmed	
Heart	heart[MH] OR myocardium[MH] OR heart[TIAB] OR hearts[TIAB] OR cardiac[TIAB] OR myocardial[TIAB] OR myocardium[TIAB] OR myocardia[TIAB] OR myocard[TIAB] OR cardioprotection[TIAB] OR cardioprotective[TIAB] OR coronary[TIAB]
Ischemia-Reperfusion Injury	ischemia[MH] OR "warm ischemia"[MH] OR "cold ischemia"[MH] OR "reperfusion injury"[MH] OR "myocardial ischemia"[MH] OR "coronary occlusion"[MH] OR "heart injuries"[MH] OR "cardiovascular diseases"[MH] OR transplantation[MH] OR "heart transplantation"[MH] OR "primary graft dysfunction"[MH] OR "graft survival"[MH] OR "graft rejection" [MH] OR transplants[MH] OR ((ischemia[TIAB] OR ischaemia[TIAB] OR ischemic[TIAB] OR ischaemic[TIAB]) AND ("reperfusion"[tiab] OR reoxygenation[tiab] OR re-oxygenation[tiab])) OR "reperfusion injury"[TIAB] OR "reperfusion injuries"[TIAB] OR "I/R"[TIAB] OR "IRI"[TIAB] OR occlusion[TIAB] OR transplantation[TIAB] OR transplantations[TIAB] OR transplant[TIAB] OR transplants[TIAB] OR graft[TIAB] OR grafts[TIAB]
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Animals	("animal experimentation"[MeSH Terms] OR "models, animal"[MeSH Terms] OR "invertebrates"[MeSH Terms] OR "Animals"[Mesh:noexp] OR "animal population groups"[MeSH Terms] OR "chordata"[MeSH Terms:noexp] OR "chordata, nonvertebrate"[MeSH Terms] OR "vertebrates"[MeSH Terms:noexp] OR "amphibians"[MeSH Terms] OR "birds"[MeSH Terms] OR "fishes"[MeSH Terms] OR "reptiles"[MeSH Terms] OR "mammals"[MeSH Terms:noexp] OR "primates"[MeSH Terms:noexp] OR "artiodactyla"[MeSH Terms] OR "carnivora"[MeSH Terms] OR "cetacea"[MeSH Terms] OR "chiroptera"[MeSH Terms] OR "elephants"[MeSH Terms] OR "hyraxes"[MeSH Terms] OR "insectivora"[MeSH Terms] OR "lagomorpha"[MeSH Terms] OR "marsupialia"[MeSH Terms] OR "monotremata"[MeSH Terms] OR "perissodactyla"[MeSH Terms] OR "rodentia"[MeSH Terms] OR "scandentia"[MeSH Terms] OR "sirenia"[MeSH Terms] OR "xenarthra"[MeSH Terms] OR "haplorhini"[MeSH Terms:noexp] OR "strepsirhini"[MeSH Terms] OR "platyrrhini"[MeSH Terms] OR "tarsii"[MeSH Terms] OR "catarrhini"[MeSH Terms:noexp] OR "cercopithecidae"[MeSH Terms] OR "hylobatidae"[MeSH Terms] OR "hominidae"[MeSH Terms:noexp] OR "gorilla gorilla"[MeSH Terms] OR "pan paniscus"[MeSH Terms] OR "pan troglodytes"[MeSH Terms] OR "pongo pygmaeus"[MeSH Terms]) OR ((animals[tiab] OR animal[tiab] OR mice[Tiab] OR mus[Tiab] OR mouse[Tiab] OR murine[Tiab] OR woodmouse[tiab] OR rats[Tiab] OR rat[Tiab] OR murinae[Tiab] OR muridae[Tiab] OR cottonrat[tiab] OR cottonrats[tiab] OR hamster[tiab] OR hamsters[tiab] OR cricetinae[tiab] OR rodentia[Tiab] OR rodent[Tiab] OR rodents[Tiab] OR pigs[Tiab] OR pig[Tiab] OR swine[tiab] OR swines[tiab] OR piglets[tiab] OR piglet[tiab] OR boar[tiab] OR boars[tiab] OR "sus scrofa"[tiab] OR ferrets[tiab] OR ferret[tiab] OR polecat[tiab] OR polecats[tiab] OR "mustela putorius"[tiab] OR "guinea pigs"[Tiab] OR "guinea

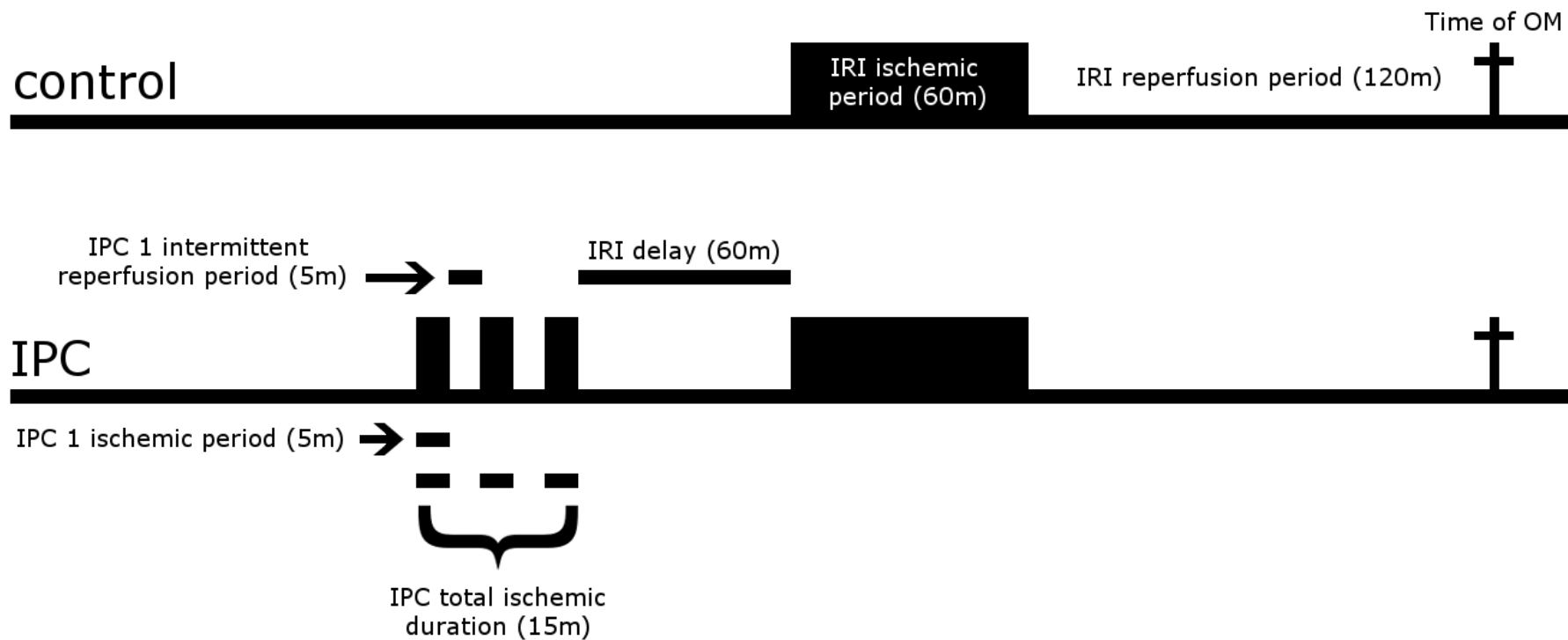
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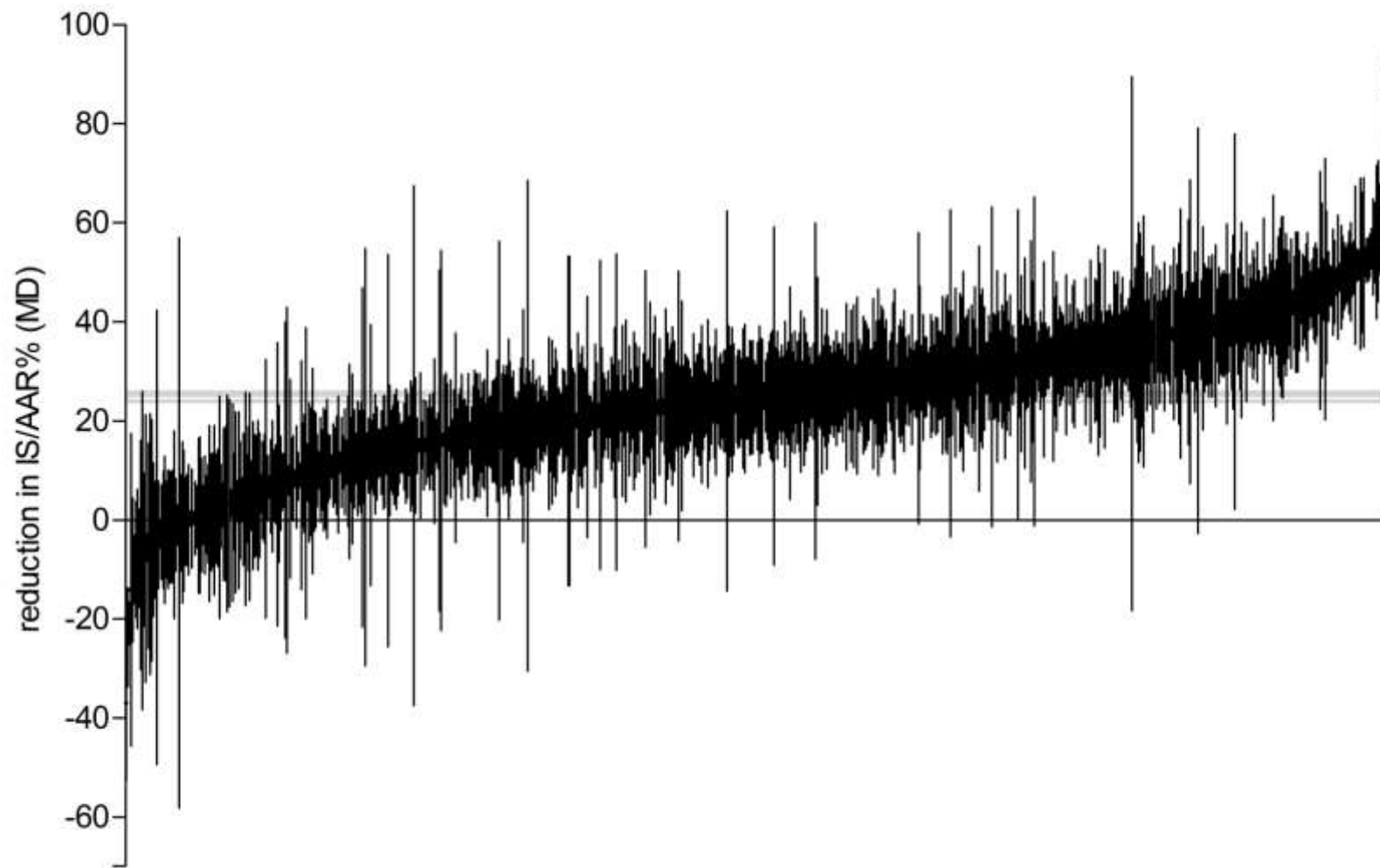
EMBASE	
Heart	exp heart/ or (heart or hearts or cardiac or myocardial or myocardium or myocardia or myocard or cardioprotection or cardioprotective or coronary).ti,ab.
Ischemia-Reperfusion Injury	exp reperfusion injury/ or exp cold ischemia/ or exp primary graft dysfunction/ or exp transplantation/ or (((ischemia or ischaemia or ischemia or ischaemia) and (reperfusion or reoxygenation or re-oxygenation)) or reperfusion injury or reperfusion injuries or I/r or IRI or occlusion or transplantation or transplantations or transplant or transplants or graft or grafts).ti,ab.
Preconditioning	exp ischemic preconditioning/ or (IPC or RIPC or brief ischemia or brief ischaemia or preconditioning or pre conditioning or pre-conditioning or transient ischaemia or transient ischemia or intermittent ischaemia or intermittent ischemia or remote conditioning).ti,ab.
Animals	exp animal experiment/ or exp animal model/ or exp experimental animal/ or exp transgenic animal/ or exp male animal/ or exp female animal/ or exp juvenile animal/ OR animal/ OR chordata/ OR vertebrate/ OR tetrapod/ OR exp fish/ OR amniote/ OR exp amphibia/ OR mammal/ OR exp reptile/ OR exp sauropsid/ OR therian/OR exp monotremate/ OR placental mammals/ OR exp marsupial/ OR Euarchontoglires/ OR exp Afrotheria/ OR exp Boreoeutheria/ OR exp Laurasiatheria/ OR exp Xenarthra/ OR primate/ OR exp Dermoptera/ OR exp Glires/ OR exp Scandentia/ OR Haplorhini/ OR exp prosimian/ OR simian/ OR exp tarsiform/ OR Catarrhini/ OR exp Platyrrhini/ OR ape/ OR exp Cercopithecidae/ OR hominid/ OR exp hylobatidae/ OR exp chimpanzee/ OR exp gorilla/ OR exp orang utan/ OR (animal OR animals OR pisces OR fish OR fishes OR catfish OR catfishes OR sheatfish OR silurus OR arius OR heteropneustes OR clarias OR gariepinus OR fathead minnow OR fathead minnows OR pimephales OR promelas OR cichlidae OR trout OR trouts OR char OR chars OR salvelinus OR salmo OR oncorhynchus OR guppy OR guppies OR millionfish OR poecilia OR goldfish OR goldfishes OR carassius OR auratus OR mullet OR mullets OR mugil OR curema OR shark OR sharks OR cod OR cods OR gadus OR morhua OR carp OR carps OR cyprinus OR carpio OR killifish OR eel OR eels OR anguilla OR zander OR sander OR lucioperca OR stizostedion OR turbot OR turbots OR psetta OR flatfish OR flatfishes OR plaice OR pleuronectes OR platessa OR tilapia OR tilapias OR oreochromis OR sarotherodon OR common sole OR dover sole OR solea OR zebrafish OR zebrafishes OR danio OR rerio OR seabass OR dicentrarchus OR labrax OR morone OR lamprey OR lampreys OR petromyzon OR pumpkinseed OR

pumpkinseeds OR lepomis OR gibbosus OR herring OR clupea OR harengus OR
amphibia OR amphibian OR amphibians OR anura OR salientia OR frog OR frogs
OR rana OR toad OR toads OR bufo OR xenopus OR laevis OR bombina OR
epidalea OR calamita OR salamander OR salamanders OR newt OR newts OR
triturus OR reptilia OR reptile OR reptiles OR bearded dragon OR pogona OR
vitticeps OR iguana OR iguanas OR lizard OR lizards OR anguis fragilis OR turtle OR
turtles OR snakes OR snake OR aves OR bird OR birds OR quail OR quails OR
coturnix OR bobwhite OR colinus OR virginianus OR poultry OR poultries OR fowl
OR fowls OR chicken OR chickens OR gallus OR zebra finch OR taeniopygia OR
guttata OR canary OR canaries OR serinus OR canaria OR parakeet OR parakeets
OR grasskeet OR parrot OR parrots OR psittacine OR psittacines OR shelduck OR
tadorna OR goose OR geese OR branta OR leucopsis OR woodlark OR lullula OR
flycatcher OR ficedula OR hypoleuca OR dove OR doves OR geopelia OR cuneata
OR duck OR ducks OR greylag OR graylag OR anser OR harrier OR circus pygargus
OR red knot OR great knot OR calidris OR canutus OR godwit OR limosa OR
lapponica OR meleagris OR gallopavo OR jackdaw OR corvus OR monedula OR ruff
OR philomachus OR pugnax OR lapwing OR peewit OR plover OR vanellus OR
swan OR cygnus OR columbianus OR bewickii OR gull OR chroicocephalus OR
ridibundus OR albifrons OR great tit OR parus OR aythya OR fuligula OR
streptopelia OR risoria OR spoonbill OR platalea OR leucorodia OR blackbird OR
turdus OR merula OR blue tit OR cyanistes OR pigeon OR pigeons OR columba OR
pintail OR anas OR starling OR sturnus OR owl OR athene noctua OR pochard OR
ferina OR cockatiel OR nymphicus OR hollandicus OR skylark OR alauda OR tern
OR sterna OR teal OR crecca OR oystercatcher OR haematopus OR ostralegus OR
shrew OR shrews OR sorex OR araneus OR crocidura OR russula OR european
mole OR talpa OR chiroptera OR bat OR bats OR eptesicus OR serotinus OR myotis
OR dasycneme OR daubentonii OR pipistrelle OR pipistrellus OR cat OR cats OR
felis OR catus OR feline OR dog OR dogs OR canis OR canine OR canines OR otter
OR otters OR lutra OR badger OR badgers OR meles OR fitchew OR fitch OR
foumart or foulmart OR ferrets OR ferret OR polecat OR polecats OR mustela OR
putorius OR weasel OR weasels OR fox OR foxes OR vulpes OR common seal OR
phoca OR vitulina OR grey seal OR halichoerus OR horse OR horses OR equus OR
equine OR equidae OR donkey OR donkeys OR mule OR mules OR pig OR pigs OR
swine OR swines OR hog OR hogs OR boar OR boars OR porcine OR piglet OR
piglets OR sus OR scrofa OR llama OR llamas OR lama OR glama OR deer OR deers
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OR bull OR bulls OR cattle OR bison OR bisons OR sheep OR sheeps OR ovis aries
OR ovine OR lamb OR lambs OR mouflon OR mouflons OR goat OR goats OR capra
OR caprine OR chamois OR rupicapra OR leporidae OR lagomorpha OR lagomorph
OR rabbit OR rabbits OR oryctolagus OR cuniculus OR laprine OR hares OR lepus
OR rodentia OR rodent OR rodents OR murinae OR mouse OR mice OR mus OR
musculus OR murine OR woodmouse OR apodemus OR rat OR rats OR rattus OR
norvegicus OR guinea pig OR guinea pigs OR cavia OR porcellus OR hamster OR
hamsters OR mesocricetus OR cricetus OR cricetus OR gerbil OR gerbils OR jird
OR jirds OR meriones OR unguiculatus OR jerboa OR jerboas OR jaculus OR
chinchilla OR chinchillas OR beaver OR beavers OR castor fiber OR castor
canadensis OR sciuridae OR squirrel OR squirrels OR sciurus OR chipmunk OR
chipmunks OR marmot OR marmots OR marmota OR suslik OR susliks OR
spermophilus OR cynomys OR cottonrat OR cottonrats OR sigmodon OR vole OR
voles OR microtus OR myodes OR glareolus OR primate OR primates OR prosimian
OR prosimians OR lemur OR lemurs OR lemuridae OR loris OR bush baby OR bush
babies OR bushbaby OR bushbabies OR galago OR galagos OR anthropoidea OR

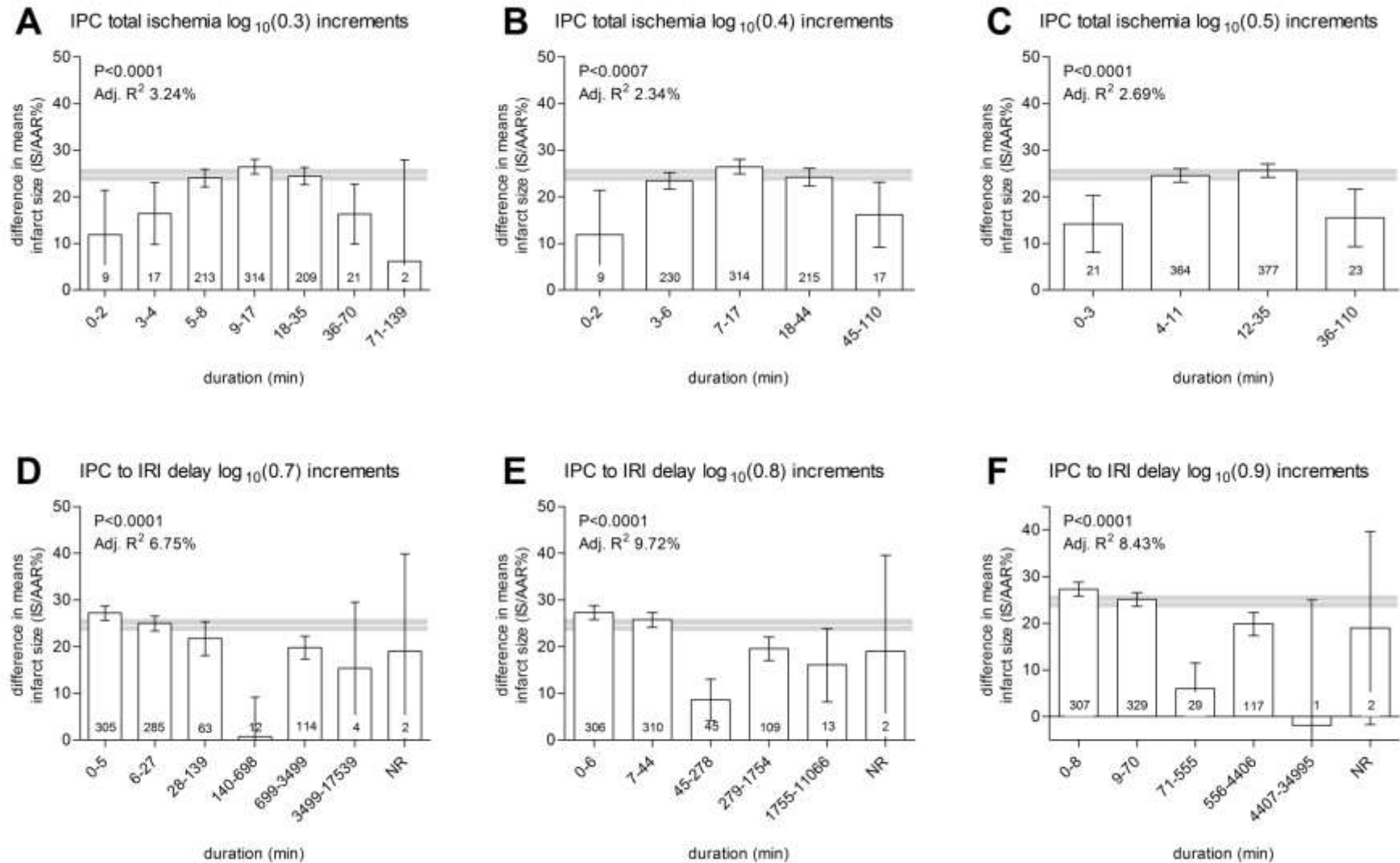
anthropoids OR simian OR simians OR monkey OR monkeys OR marmoset OR marmosets OR callithrix OR cebuella OR tamarin OR tamarins OR saguinus OR leontopithecus OR squirrel monkey OR squirrel monkeys OR saimiri OR night monkey OR night monkeys OR owl monkey OR owl monkeys OR douroucoulis OR aotus OR spider monkey OR spider monkeys OR ateles OR baboon OR baboons OR papio OR rhesus monkey OR macaque OR macaca OR mulatta OR cynomolgus OR fascicularis OR green monkey OR green monkeys OR chlorocebus OR vervet OR vervets OR pygerythrus OR hominoidea OR ape OR apes OR hylobatidae OR gibbon OR gibbons OR siamang OR siamangs OR nomascus OR symphalangus OR hominidae OR orangutan OR orangutans OR pongo OR chimpanzee OR chimpanzees OR pan troglodytes OR bonobo OR bonobos OR pan paniscus OR gorilla OR gorillas OR troglodytes).ti,ab.



Supplemental Figure A| Ischemia-reperfusion injury (IRI) and ischemic preconditioning (IPC) characteristics for a typical control and experimental group. Control animals undergo a waiting period, followed by 60 minutes of coronary occlusion (ischemic period) and 120 minutes of reperfusion. In the experimental group, the applied IPC protocol consists of 3 cycles of 5 minutes of ischemia, interspersed by 5 minutes of reperfusion. The total duration of IPC ischemia is 15 minutes. The delay to myocardial IRI in this protocol is 60 minutes.



Supplemental Figure B | Individual effect estimates of all 785 included comparisons. Data are presented as raw difference in means (MD) in infarct size as a percentage of the area at risk (IS/AAR%). Comparisons are sorted by MD from low to high. The vertical error bars represent the 95% confidence intervals for the individual estimates. Horizontal white line and grey bar represent the pooled effect estimate and its 95% confidence interval.



Supplemental Figure C| Sensitivity analysis total duration IPC ischemia (A-C) and IPC to IRI delay (D-F). Data are presented as raw difference in means (MD) in infarct size as a percentage of the area at risk (IS/AAR%). Horizontal white line and grey bar represent the pooled effect estimate and its 95% confidence interval. The number of comparisons contributing data is indicated in each bar. Panels B and D represent the original subgroups, other panels represent alternative subgroups based on slightly smaller (A and D) or larger (C and F) log increments.

Supplemental table A - study and comparison characteristics - page 1 of 26

comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Alcindor2004 ¹	dog	NR	m/f	none	local	NA	4	5	20	5
Alizadeh2011 ²	rat	NR	m	none	local	NA	1	5	5	5
Alkhulaifi1993_ip0.5 ³	rat	NR	m	none	local	NA	1	5	5	0.5
Alkhulaifi1993_ip1 ³	rat	NR	m	none	local	NA	1	5	5	1
Amour2009 ⁴	rabbit	NR	m	none	local	NA	1	5	5	15
Andreadou2004 ⁵	rabbit	NR	m	none	local	NA	2	5	10	10
Andreadou2006 ⁶	rabbit	NR	m	none	local	NA	2	5	10	10
Andreadou2011_1cy ⁷	rabbit	NR	m	none	local	NA	1	5	5	10
Andreadou2011_4cy ⁷	rabbit	NR	m	none	local	NA	4	4	16	10
Aouam2005_1cy ⁸	rabbit	NR	m	none	local	NA	1	5	5	10
Aouam2005_6cy ⁸	rabbit	NR	m	none	local	NA	6	4	24	4
Argaud2004 ⁹	rabbit	yes	m	none	local	NA	1	5	5	5
Argaud2005a ¹⁰	rabbit	yes	m	none	local	NA	1	5	5	5
Argaud2005b ¹¹	rabbit	NR	m	none	local	NA	1	5	5	5
Argaud2005c ¹²	rabbit	NR	m	none	local	NA	1	5	5	5
Argaud2008 ¹³	rabbit	NR	m	none	local	NA	1	5	5	5
Auchampach1992 ¹⁴	dog	NR	m/f	none	local	NA	1	5	5	10
Auchampach1993 ¹⁵	dog	NR	m/f	none	local	NA	1	5	5	10
Auchampach2004 ¹⁶	dog	NR	m/f	none	local	NA	4	5	20	10
Aye1999_1cy ¹⁷	rat	NR	m	none	local	NA	1	3	3	10
Aye1999_3cy ¹⁷	rat	NR	m	none	local	NA	3	3	9	5
Baines1997_1cy ¹⁸	rabbit	NR	m/f	none	local	NA	1	5	5	10
Baines1997_4cy ¹⁸	rabbit	NR	m/f	none	local	NA	4	5	20	10
Baines1999 ¹⁹	rabbit	NR	m/f	none	local	NA	1	5	5	10
Barbosa1996_01.25ip ²⁰	rat	NR	f	none	local	NA	1	1	1	5
Barbosa1996_02.5ip ²⁰	rat	NR	f	none	local	NA	1	3	3	5
Barbosa1996_05ip ²⁰	rat	NR	f	none	local	NA	1	5	5	5
Barbosa1996_10ip ²⁰	rat	NR	f	none	local	NA	1	10	10	5
Barbosa1996_2cy ²⁰	rat	NR	f	none	local	NA	2	5	10	5
Barbosa1996_2cy10ip ²⁰	rat	NR	f	none	local	NA	2	10	20	5
Barbosa1996_4cy ²⁰	rat	NR	f	none	local	NA	4	5	20	5

Supplemental table A - study and comparison characteristics - page 2 of 26

comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Basalay2012_exp1 ²¹	rat	NR	m	none	remote	hind limb	1	15	15	10
Basalay2012_exp2 ²¹	rat	NR	m	none	remote	hind limb	1	15	15	10
Basalay2012_exp3 ²¹	rat	NR	m	none	remote	hind limb	1	15	15	10
Baumert2007 ²²	pig	NR	NR	none	local	NA	4	5	20	5
Baxter1994 ²³	rabbit	yes	m	none	local	NA	4	5	20	1440
Baxter1995 ²⁴	rabbit	yes	m	none	local	NA	4	5	20	1440
Baxter1997_1cy ²⁵	rabbit	yes	m	none	local	NA	1	5	5	2880
Baxter1997_2cy ²⁵	rabbit	yes	m	none	local	NA	2	5	10	2880
Baxter1997_4cy ²⁵	rabbit	yes	m	none	local	NA	4	5	20	2880
Baxter1997_ip24h ²⁵	rabbit	yes	m	none	local	NA	4	5	20	1440
Baxter1997_ip48h ²⁵	rabbit	yes	m	none	local	NA	4	5	20	2880
Baxter1997_ip72h ²⁵	rabbit	yes	m	none	local	NA	4	5	20	4320
Baxter1997_ip96h ²⁵	rabbit	yes	m	none	local	NA	4	5	20	5760
Belosjorow1999 ²⁶	rabbit	NR	NR	none	local	NA	1	5	5	10
Belosjorow2003 ²⁷	rabbit	NR	NR	none	local	NA	1	5	5	10
Bencsik2010 ²⁸	rat	NR	NR	none	local	NA	5	4	20	1440
Bernardo1999 ²⁹	rabbit	NR	m	none	local	NA	4	5	20	1440
Bibli2013 ³⁰	rabbit	NR	m	none	local	NA	2	5	10	10
Blokhin2008a ³¹	rat	NR	m	none	local	NA	1	5	5	5
Blokhin2008b_20is ³²	rat	NR	m	none	local	NA	3	5	15	5
Blokhin2008b_30is ³²	rat	NR	m	none	local	NA	3	5	15	5
Blokhin2008b_40is ³²	rat	NR	m	none	local	NA	3	5	15	5
Blokhin2008b_50is ³²	rat	NR	m	none	local	NA	3	5	15	5
Blokhin2008b_60is ³²	rat	NR	m	none	local	NA	3	5	15	5
Boengler2007_old ³³	mouse	NR	m/f	senescence	local	NA	1	10	10	10
Boengler2007_young ³³	mouse	NR	m/f	none	local	NA	1	10	10	10
Brandenburger2012 ³⁴	rat	NR	NR	none	remote	hind limb	4	5	20	5
Bukhari1995 ³⁵	sheep	NR	m/f	none	local	NA	3	5	15	5
Burckhartt1995_ip2h ³⁶	rabbit	NR	NR	none	local	NA	1	5	5	120
Burckhartt1995_ip4h ³⁶	rabbit	NR	NR	none	local	NA	1	5	5	240
Burns1996_adult ³⁷	sheep	NR	m/f	none	local	NA	3	5	15	5

Supplemental table A - study and comparison characteristics - page 3 of 26

comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Burns1996_old ³⁷	sheep	NR	m/f	senescence	local	NA	3	5	15	5
Cai2008 ³⁸	mouse	NR	m	none	local	NA	1	10	10	5
Cai2013 ³⁹	mouse	NR	m	none	remote	hind limb	3	5	15	1440
Canyon2005 ⁴⁰	rat	NR	m	none	local	NA	3	3	9	3
Cason1997 ⁴¹	rabbit	NR	NR	none	local	NA	1	5	5	15
Chazov2001 ⁴²	rat	NR	m	none	local	NA	3	5	15	5
Chen1997 ⁴³	rabbit	NR	m	none	local	NA	4	5	20	10
Chen2005 ⁴⁴	rat	NR	NR	none	remote	hind limb	4	5	20	5
Chen2008 ⁴⁵	rat	NR	m	none	local	NA	2	3	6	5
Cheng2009 ⁴⁶	rat	NR	m	none	local	NA	3	5	15	5
Cheng2010a ⁴⁷	rat	NR	m	none	local	NA	4	5	20	5
Cheng2010b ⁴⁸	rat	NR	m	none	local	NA	4	5	20	5
Chiari2002 ⁴⁹	rabbit	yes	m/f	brain death	local	NA	2	5	10	10
Chien1996 ⁵⁰	rabbit	NR	m	none	local	NA	1	5	5	10
Chien1999 ⁵¹	rabbit	NR	m	none	local	NA	1	5	5	10
Cohen1991 ⁵²	rabbit	NR	NR	none	local	NA	1	5	5	10
Cohen1994_1cy ⁵³	rabbit	none	NR	none	local	NA	1	5	5	10
Cohen1994_rep ⁵³	rabbit	none	NR	none	local	NA	12	5	60	10
Cohen1994_rep+1cy ⁵³	rabbit	none	NR	none	local	NA	12	5	60	10
Cohen1999 ⁵⁴	rabbit	yes	m/f	none	local	NA	1	5	5	10
Cohen2000 ⁵⁵	rabbit	yes	m/f	none	local	NA	1	5	5	10
Colantonio2004 ⁵⁶	dog	NR	NR	none	local	NA	1	10	10	10
Dai2003 ⁵⁷	rat	NR	f	none	local	NA	3	3	9	5
Dai2009_healthy ⁵⁸	rat	NR	f	none	local	NA	3	3	9	5
Dai2009_hyperten ⁵⁸	rat	NR	f	hypertension	local	NA	3	3	9	5
Dairaku2002 ⁵⁹	rat	NR	m	none	local	NA	3	3	9	3
Daleau2001_120is ⁶⁰	rabbit	NR	m	none	local	NA	2	5	10	10
Daleau2001_30is ⁶⁰	rabbit	NR	m	none	local	NA	2	5	10	10
Das2006 ⁶¹	rabbit	NR	m	none	local	NA	1	5	5	10
Das2007 ⁶²	rabbit	NR	m	none	local	NA	1	5	5	10
Das2012 ⁶³	rabbit	NR	m	none	local	NA	1	5	5	10

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Dawn2002 ⁶⁴	rabbit	NR	m	none	local	NA	6	4	24	1440
Dawn2004a ⁶⁵	mouse	NR	NR	none	local	NA	6	4	24	1440
Dawn2004b ⁶⁶	mouse	NR	NR	none	local	NA	6	4	24	1440
Demiryurek2005a ⁶⁷	rat	NR	m	none	local	NA	1	5	5	5
Demiryurek2005b ⁶⁸	rat	NR	m	none	local	NA	1	5	5	5
DePaulis2013 ⁶⁹	rat	NR	m	none	local	NA	3	3	9	5
Depre2010_ip24h ⁷⁰	pig	NR	NR	none	local	NA	2	10	20	1440
Depre2010_ip60 ⁷⁰	pig	NR	NR	none	local	NA	6	10	60	60
Deuchar2007 ⁷¹	rat	NR	m	none	local	NA	3	3	9	5
DeZeeuw2001_10ip ⁷²	pig	NR	m/f	none	remote	brain	1	10	10	20
DeZeeuw2001_30ip ⁷²	pig	NR	m/f	none	remote	brain	1	30	30	30
Ding2000 ⁷³	rabbit	NR	m	none	local	NA	2	5	10	10
Ding2001 ⁷⁴	rabbit	NR	m	none	remote	RAO	1	10	10	10
Dong2004 ⁷⁵	rat	NR	m	none	remote	hind limb	1	10	10	10
Ebel2003_diabetic ⁷⁶	rabbit	NR	m	diabetes	local	NA	1	5	5	1440
Ebel2003_healthy1 ⁷⁶	rabbit	NR	m	none	local	NA	1	5	5	1440
Ebel2003_healthy2 ⁷⁶	rabbit	NR	m	none	local	NA	1	5	5	1440
Ebel2003_hypergly ⁷⁶	rabbit	NR	m	hyperglycaemia	local	NA	1	5	5	1440
Ebel2009_diabetic ⁷⁷	rat	NR	m	diabetes	local	NA	3	3	9	5
Ebel2009_healthy ⁷⁷	rat	NR	m	none	local	NA	3	3	9	5
Eckle2006_1cy ⁷⁸	mouse	NR	m/f	none	local	NA	1	5	5	5
Eckle2006_2cy ⁷⁸	mouse	NR	m/f	none	local	NA	2	5	10	5
Eckle2006_3cy ⁷⁸	mouse	NR	m/f	none	local	NA	3	5	15	5
Eckle2006_4cy ⁷⁸	mouse	NR	m/f	none	local	NA	4	5	20	5
Eckle2012 ⁷⁹	mouse	NR	m	none	local	NA	4	5	20	5
Erikson1996 ⁸⁰	dog	NR	NR	none	local	NA	4	5	20	5
Fang2008 ⁸¹	rat	NR	m	none	local	NA	3	5	15	5
Farhat2001_braindead ⁸²	rabbit	NR	NR	brain death	local	NA	1	5	5	5
Farhat2001_healthy ⁸²	rabbit	NR	NR	none	local	NA	1	5	5	5
Fisher2002_ip15m ⁸³	mouse	NR	m	none	local	NA	3	5	15	15
Fisher2002_ip24h ⁸³	mouse	NR	m	none	local	NA	3	5	15	1440

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Flack3rd1991 ⁸⁴	pig	NR	m/f	none	local	NA	4	5	20	5
Flaherty2008 ⁸⁵	mouse	NR	m	none	local	NA	6	4	24	4
Flynn2005_1cy ⁸⁶	rabbit	NR	m	none	local	NA	1	5	5	10
Flynn2005_2cy ⁸⁶	rabbit	NR	m	none	local	NA	1	5	5	10
Fryer1998 ⁸⁷	rat	NR	m	none	local	NA	1	5	5	5
Fryer1999_1cy ⁸⁸	rat	NR	m	none	local	NA	1	5	5	5
Fryer1999_3cy ⁸⁸	rat	NR	m	none	local	NA	3	5	15	5
Fryer2000 ⁸⁹	rat	NR	m	none	local	NA	1	5	5	5
Fryer2001a ⁹⁰	rat	NR	m	none	local	NA	1	5	5	5
Fryer2001b ⁹¹	rat	NR	m	none	local	NA	1	5	5	5
Fryer2001c ⁹²	rat	NR	m	none	local	NA	1	5	5	5
Fryer2002 ⁹³	rat	NR	m	none	local	NA	1	5	5	5
Fukuma2000 ⁹⁴	rabbit	NR	m	none	local	NA	1	5	5	5
Galagudza2007a_diabetic ⁹⁵	rat	NR	m	diabetes	local	NA	1	5	5	5
Galagudza2007a_healthy ⁹⁵	rat	NR	m	none	local	NA	1	5	5	5
Galagudza2007b_1cy ⁹⁶	rat	NR	m	none	local	NA	1	5	5	5
Galagudza2007b_3cy ⁹⁶	rat	NR	m	none	local	NA	3	5	15	5
Galagudza2007b_RIPC ⁹⁶	rat	NR	m	none	remote	MAO	1	5	5	15
Galagudza2009 ⁹⁷	rat	NR	m	none	local	NA	3	4	12	5
Gao2000 ⁹⁸	mouse	NR	m/f	none	local	NA	3	5	15	10
Gao2003_ip10 ⁹⁹	rat	NR	m	none	local	NA	3	5	15	10
Gao2003_ip24h ⁹⁹	rat	NR	m	none	local	NA	3	5	15	1440
Gao2012_IPC ¹⁰⁰	rat	NR	m	none	local	NA	3	5	15	5
Gao2012_RIPC ¹⁰⁰	rat	NR	m	none	remote	hind limb	3	5	15	5
Ge2011_exp1 ¹⁰¹	mouse	NR	NR	hyperglycaemia	local	NA	4	5	20	5
Ge2011_exp2 ¹⁰¹	mouse	NR	NR	hyperglycaemia	local	NA	4	5	20	5
Gerczuk2012 ¹⁰²	rat	NR	m	none	local	NA	3	3	9	5
Gho1996_IPC ¹⁰³	rat	NR	m	none	local	NA	1	15	15	10
Gho1996_MAO ¹⁰³	rat	NR	m	none	remote	MAO	1	15	15	10
Gho1996_RAO ¹⁰³	rat	NR	m	none	remote	RAO	1	15	15	10
Gomez2011 ¹⁰⁴	mouse	yes	m	none	local	NA	1	5	5	5

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Gomoll1996_02ip ¹⁰⁵	ferret	NR	m	none	local	NA	1	2	2	10
Gomoll1996_05ip ¹⁰⁵	ferret	NR	m	none	local	NA	1	5	5	10
Gomoll1996_10ip ¹⁰⁵	ferret	NR	m	none	local	NA	1	10	10	10
Gomoll1996_75is ¹⁰⁵	ferret	NR	m	none	local	NA	1	5	5	10
Gomoll1996_90is ¹⁰⁵	ferret	NR	m	none	local	NA	1	5	5	10
Goto1993 ¹⁰⁶	rabbit	NR	m	none	local	NA	2	2	4	5
Gourine2005 ¹⁰⁷	rat	NR	m	none	local	NA	3	5	15	5
Gozal2005 ¹⁰⁸	rabbit	NR	NR	none	local	NA	1	5	5	10
Griol-Charhbili2005 ¹⁰⁹	mouse	NR	m	none	local	NA	3	3	9	5
Gross1992 ¹¹⁰	dog	NR	m/f	none	local	NA	1	5	5	10
Gross2009 ¹¹¹	dog	NR	m/f	none	local	NA	1	5	5	10
Grover1992 ¹¹²	dog	NR	m/f	none	local	NA	1	5	5	10
Grover1996 ¹¹³	dog	NR	m/f	none	local	NA	1	5	5	10
Grund1997_1cy ¹¹⁴	pig	NR	m/f	none	local	NA	1	10	10	30
Grund1997_2cy ¹¹⁴	pig	NR	m/f	none	local	NA	2	10	20	30
Gu2008 ¹¹⁵	dog	NR	m/f	hyperglycaemia	local	NA	4	5	20	5
Gumina1999_1cy ¹¹⁶	dog	NR	m/f	none	local	NA	1	5	5	10
Gumina1999_4cy ¹¹⁶	dog	NR	m/f	none	local	NA	4	5	20	5
Gumina1999_60is ¹¹⁶	dog	NR	m/f	none	local	NA	1	5	5	10
Gumina2001 ¹¹⁷	dog	NR	m/f	none	local	NA	1	5	5	10
Gumina2005_1cy ¹¹⁸	dog	NR	m/f	none	local	NA	1	10	10	10
Gumina2005_1cyip2h ¹¹⁸	dog	NR	m/f	none	local	NA	1	10	10	120
Gumina2005_2cy ¹¹⁸	dog	NR	m/f	none	local	NA	2	10	20	10
Guo1998_early ¹¹⁹	mouse	NR	m	none	local	NA	6	4	24	10
Guo1998_late24hR ¹¹⁹	mouse	NR	m	none	local	NA	6	4	24	1440
Guo1998_late4R ¹¹⁹	mouse	NR	m	none	local	NA	6	4	24	1440
Guo1999_ip10 ¹²⁰	mouse	NR	m	none	local	NA	6	4	24	10
Guo1999_ip24h ¹²⁰	mouse	NR	m	none	local	NA	6	4	24	1440
Guo2001_1cy ¹²¹	mouse	NR	m	none	local	NA	1	4	4	10
Guo2001_6cy ¹²¹	mouse	NR	m	none	local	NA	6	4	24	4
Guo2007 ¹²²	rat	NR	NR	none	local	NA	2	5	10	5

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Guo2012_exp1 ¹²³	mouse	NR	m	none	local	NA	6	4	24	1440
Guo2012_exp2 ¹²³	mouse	NR	m	none	local	NA	6	4	24	1440
Guo2012_exp3 ¹²³	mouse	NR	m	none	local	NA	6	4	24	1440
Gysembergh1998 ¹²⁴	rabbit	yes	NR	none	local	NA	1	5	5	5
Haessler1994_iso ¹²⁵	rabbit	NR	NR	none	local	NA	1	5	5	10
Haessler1994_kxy ¹²⁵	rabbit	NR	NR	none	local	NA	1	5	5	10
Haessler1994_pen ¹²⁵	rabbit	NR	NR	none	local	NA	1	5	5	10
Haessler1997 ¹²⁶	rabbit	NR	NR	none	local	NA	1	5	5	10
Hale1992_exp1 ¹²⁷	rabbit	NR	m	none	local	NA	2	5	10	5
Hale1992_exp2 ¹²⁷	rabbit	NR	m	none	local	NA	2	5	10	5
Hale1999_1cy ¹²⁸	rabbit	NR	NR	none	local	NA	1	5	5	5
Hale1999_2cy ¹²⁸	rabbit	NR	NR	none	local	NA	2	7	14	5
Halkos2004 ¹²⁹	dog	yes	NR	none	local	NA	1	5	5	10
Hampton2003 ¹³⁰	mouse	NR	NR	none	local	NA	3	5	15	1440
Haruna1998 ¹³¹	rabbit	NR	f	none	local	NA	1	5	5	10
Hatori2001 ¹³²	pig	NR	m/f	none	local	NA	1	5	5	15
Hausenloy2012 ¹³³	pig	yes	NR	none	remote	hind limb	4	5	20	5
He2009 ¹³⁴	rabbit	NR	f	none	local	NA	3	5	15	5
Heinen2011_IPC ¹³⁵	rat	NR	m	none	local	NA	4	5	20	5
Heinen2011_IPC+RIPC ¹³⁵	rat	NR	m	none	local+remote	hind limb	4	5	20	5
Heinen2011_RIPC ¹³⁵	rat	NR	m	none	remote	hind limb	4	5	20	5
HemetsbergerH2008 ¹³⁶	pig	NR	NR	none	local	NA	2	5	10	5
HemetsbergerR2008 ¹³⁷	pig	NR	NR	none	local	NA	2	5	10	5
Hiasa2001 ¹³⁸	rat	NR	m	none	local	NA	4	5	20	10
Hibert2013 ¹³⁹	rat	NR	m	none	remote	hind limb	1	10	10	10
Hide1996 ¹⁴⁰	rabbit	yes	m	none	local	NA	1	5	5	15
Hinokiyama2003 ¹⁴¹	pig	NR	m/f	none	local	NA	1	5	5	15
Hiroi2010_1ip ¹⁴²	rat	NR	m	none	local	NA	4	1	4	1440
Hiroi2010_3ip ¹⁴²	rat	NR	m	none	local	NA	4	3	12	1440
Hoshida1994 ¹⁴³	dog	NR	m/f	none	local	NA	4	5	20	5
Htun1998 ¹⁴⁴	pig	yes	m	none	local	NA	2	10	20	30

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Hu2002_adult ¹⁴⁵	rat	NR	m	none	remote	MAO	6	4	24	1440
Hu2002_old ¹⁴⁵	rat	NR	m	senescence	remote	MAO	6	4	24	1440
Huang1999 ¹⁴⁶	pig	NR	NR	none	local	NA	2	10	20	10
Huang2004 ¹⁴⁷	rabbit	NR	NR	none	local	NA	2	10	20	10
Huang2011 ¹⁴⁸	rabbit	NR	NR	none	local	NA	2	10	20	10
Huang2013 ¹⁴⁹	rat	NR	NR	none	local	NA	2	10	20	10
Iliodromitis1994_1cy10 ¹⁵⁰	rabbit	NR	m/f	none	local	NA	1	5	5	10
Iliodromitis1994_1cy60 ¹⁵⁰	rabbit	NR	m/f	none	local	NA	1	5	5	60
Iliodromitis1994_2cy ¹⁵⁰	rabbit	NR	m/f	none	local	NA	2	5	10	60
Iliodromitis1994_3cy ¹⁵⁰	rabbit	NR	m/f	none	local	NA	3	5	15	10
Iliodromitis1996a_1ip ¹⁵¹	rabbit	NR	NR	none	local	NA	1	1	1	10
Iliodromitis1996a_5ip ¹⁵¹	rabbit	NR	NR	none	local	NA	1	5	5	10
Iliodromitis1996b_2cy45 ¹⁵²	rabbit	NR	NR	none	local	NA	2	5	10	10
Iliodromitis1996b_2cy60 ¹⁵²	rabbit	NR	NR	none	local	NA	2	5	10	10
Iliodromitis1996b_2cy75 ¹⁵²	rabbit	NR	NR	none	local	NA	2	5	10	10
Iliodromitis1996b_ip60 ¹⁵²	rabbit	NR	NR	none	local	NA	1	5	5	60
Iliodromitis1996b_ip65 ¹⁵²	rabbit	NR	NR	none	local	NA	1	5	5	65
Iliodromitis1996b_ip70 ¹⁵²	rabbit	NR	NR	none	local	NA	1	5	5	70
Iliodromitis1996b_ip75 ¹⁵²	rabbit	NR	NR	none	local	NA	1	5	5	75
Iliodromitis1996b_ip80 ¹⁵²	rabbit	NR	NR	none	local	NA	1	5	5	80
Iliodromitis1997_1cy ¹⁵³	rabbit	NR	NR	none	local	NA	1	5	5	10
Iliodromitis1997_2cy ¹⁵³	rabbit	NR	NR	none	local	NA	2	5	10	10
Iliodromitis1997_4cy ¹⁵³	rabbit	NR	NR	none	local	NA	4	5	20	10
Iliodromitis1997_6cy ¹⁵³	rabbit	NR	NR	none	local	NA	6	5	30	10
Iliodromitis1997_8cy ¹⁵³	rabbit	NR	NR	none	local	NA	8	5	40	10
Iliodromitis2002a_1cy ¹⁵⁴	rabbit	NR	m	none	local	NA	1	5	5	10
Iliodromitis2002a_3cy ¹⁵⁴	rabbit	NR	m	none	local	NA	3	5	15	10
Iliodromitis2002b ¹⁵⁵	rabbit	NR	m	none	local	NA	1	5	5	10
Iliodromitis2003_3cy ¹⁵⁶	rabbit	NR	m	none	local	NA	3	5	15	10
Iliodromitis2003_3cy90 ¹⁵⁶	rabbit	NR	m	none	local	NA	3	5	15	90
Iliodromitis2003_8cy ¹⁵⁶	rabbit	NR	m	none	local	NA	8	5	40	10

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Iliodromitis2004 ¹⁵⁷	rabbit	NR	m	none	local	NA	3	5	15	10
Iliodromitis2006a ¹⁵⁸	rabbit	NR	m	none	local	NA	2	5	10	10
Iliodromitis2006b_exp1 ¹⁵⁹	rabbit	NR	m	hypercholesterolemia	local	NA	2	5	10	10
Iliodromitis2006b_exp2 ¹⁵⁹	rabbit	NR	m	hypercholesterolemia	local	NA	2	5	10	10
Iliodromitis2008_3cy ¹⁶⁰	rabbit	NR	m	none	local	NA	3	5	15	10
Iliodromitis2008_8cy ¹⁶⁰	rabbit	NR	m	none	local	NA	8	5	40	10
Iliodromitis2013_20ip ¹⁶¹	rabbit	NR	m	none	local	NA	1	20	20	12
Iliodromitis2013_5ip+20ip ¹⁶¹	rabbit	NR	m	none	local	NA	3	10	30	12
Iliodromitis2013_5ip20is ¹⁶¹	rabbit	NR	m	none	local	NA	2	5	10	10
Iliodromitis2013_5ip40is ¹⁶¹	rabbit	NR	m	none	local	NA	2	5	10	10
Imagawa1997 ¹⁶²	rabbit	yes	m	none	local	NA	4	5	20	2880
Imagawa1998 ¹⁶³	rabbit	yes	m	none	local	NA	1	5	5	10
Imagawa1999 ¹⁶⁴	rabbit	yes	m	none	local	NA	4	5	20	2880
Ismaeil1999 ¹⁶⁵	rabbit	NR	NR	none	local	NA	1	5	5	15
Iwamoto1991 ¹⁶⁶	rabbit	NR	m	none	local	NA	4	5	20	5
Jaberansari2001_2cy ¹⁶⁷	pig	NR	m/f	none	local	NA	2	5	10	1440
Jaberansari2001_4cy ¹⁶⁷	pig	NR	m/f	none	local	NA	4	5	20	1440
Jancso2004_2cy ¹⁶⁸	pig	NR	m/f	none	local	NA	2	2	4	1440
Jancso2004_4cy ¹⁶⁸	pig	NR	m/f	none	local	NA	4	5	20	1440
Jansco2005 ¹⁶⁹	rabbit	NR	NR	none	local	NA	4	5	20	1440
Ji2013_diabetic ¹⁷⁰	rat	NR	m	diabetes	local	NA	2	5	10	5
Ji2013_healthy ¹⁷⁰	rat	NR	m	none	local	NA	2	5	10	5
Jiao2002 ¹⁷¹	rat	NR	m	none	local	NA	2	5	10	10
Jung2000_healthy ¹⁷²	rabbit	NR	m	none	local	NA	2	5	10	10
Jung2000_hyperchol ¹⁷²	rabbit	NR	m	hypercholesterolemia	local	NA	2	5	10	10
Junhua1997 ¹⁷³	rabbit	NR	NR	none	local	NA	4	5	20	1440
Kalakech2013_mouse ¹⁷⁴	mouse	NR	m	none	remote	hind limb	4	5	20	5
Kalakech2013_rat ¹⁷⁴	rat	NR	m	none	remote	hind limb	4	5	20	5
Kapadia1997 ¹⁷⁵	pig	NR	NR	none	local	NA	2	10	20	15
Kara 2004 ¹⁷⁶	rat	NR	m	none	local	NA	1	5	5	5
Kara2006 ¹⁷⁷	rat	NR	m	none	local	NA	1	5	5	5

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Kariya1997 ¹⁷⁸	rabbit	NR	m	none	local	NA	1	5	5	5
Katakam2007_lean ¹⁷⁹	rat	NR	m	none	local	NA	1	5	5	5
Katakam2007_obese ¹⁷⁹	rat	NR	m	obese	local	NA	1	5	5	5
Kersten1997 ¹⁸⁰	dog	NR	NR	none	local	NA	4	5	20	5
Kersten1998 ¹⁸¹	dog	NR	NR	hyperglycaemia	local	NA	4	5	20	5
Kersten2000_diabetic ¹⁸²	dog	NR	NR	diabetes	local	NA	4	5	20	5
Kersten2000_healthy ¹⁸²	dog	NR	NR	none	local	NA	4	5	20	5
Kingma1999 ¹⁸³	rabbit	NR	m	none	local	NA	2	5	10	10
Kingma2011 ¹⁸⁴	dog	yes	m/f	none	remote	RAO	4	5	20	5
Kingma2013 ¹⁸⁵	dog	yes	m/f	none	local	NA	4	5	20	5
Kirsch2000_braindead ¹⁸⁶	rabbit	NR	NR	brain death	local	NA	1	3	3	3
Kirsch2000_healthy ¹⁸⁶	rabbit	NR	NR	none	local	NA	1	3	3	3
Kis2003 ¹⁸⁷	rabbit	yes	m	none	local	NA	4	5	20	1440
Kitakaze1994a ¹⁸⁸	dog	NR	NR	none	local	NA	4	5	20	5
Kitakaze1994b_anesth ¹⁸⁹	dog	NR	NR	none	local	NA	4	5	20	5
Kitakaze1994b_conscious ¹⁸⁹	dog	NR	NR	none	local	NA	4	5	20	5
Kitakaze1996a ¹⁹⁰	dog	NR	NR	none	local	NA	4	5	20	5
Kitakaze1996b ¹⁹¹	dog	NR	NR	none	local	NA	4	5	20	5
Kitakaze2000 ¹⁹²	dog	NR	NR	none	local	NA	4	5	20	5
Kocoglu2008 ¹⁹³	rat	NR	m	none	local	NA	1	5	5	5
Kohler2007 ¹⁹⁴	mouse	NR	NR	none	local	NA	4	5	20	5
Kojima1995 ¹⁹⁵	rat	NR	m	none	local	NA	1	5	5	10
Kolettis2013 ¹⁹⁶	rat	NR	m	none	local	NA	2	5	10	10
Koneru2007 ¹⁹⁷	rat	NR	m	none	local	NA	4	4	16	4
Koning1994a_ip120 ¹⁹⁸	pig	NR	NR	none	local	NA	1	10	10	120
Koning1994a_ip15 ¹⁹⁸	pig	NR	NR	none	local	NA	1	10	10	15
Koning1994a_ip180 ¹⁹⁸	pig	NR	NR	none	local	NA	1	10	10	180
Koning1994a_ip240 ¹⁹⁸	pig	NR	NR	none	local	NA	1	10	10	240
Koning1994a_ip60 ¹⁹⁸	pig	NR	NR	none	local	NA	1	10	10	60
Koning1994b_ip15 ¹⁹⁹	pig	NR	NR	none	local	NA	1	10	10	15
Koning1994b_ip60 ¹⁹⁹	pig	NR	NR	none	local	NA	1	10	10	60

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Kositprapa2001 ²⁰⁰	rabbit	NR	m	none	local	NA	4	5	20	1440
Kouchi1998 ²⁰¹	rabbit	NR	f	none	local	NA	1	5	5	10
Kremastinos2000_healthy ²⁰²	rabbit	NR	m	none	local	NA	1	5	5	10
Kremastinos2000_hyperchol ²⁰²	rabbit	NR	m	hypercholesterolemia	local	NA	1	5	5	10
Kristensen2004 ²⁰³	pig	NR	NR	none	local	NA	2	10	20	30
Kudej2006_ip10 ²⁰⁴	pig	yes	NR	none	local	NA	2	10	20	10
Kudej2006_ip24h ²⁰⁴	pig	yes	NR	none	local	NA	2	10	20	1440
Kunuthur2012_exp1 ²⁰⁵	mouse	NR	m	none	local	NA	1	5	5	5
Kunuthur2012_exp2 ²⁰⁵	mouse	NR	m	none	local	NA	1	5	5	5
Kuzmin2000 ²⁰⁶	rat	NR	m	none	local	NA	3	5	15	5
Kuzume2004_1cy ²⁰⁷	rabbit	NR	NR	none	local	NA	1	5	5	10
Kuzume2004_2cy ²⁰⁷	rabbit	NR	NR	none	local	NA	2	5	10	10
Kuzuya1993_ip03h ²⁰⁸	dog	NR	m/f	none	local	NA	4	5	20	1440
Kuzuya1993_ip05 ²⁰⁸	dog	NR	m/f	none	local	NA	4	5	20	5
Kuzuya1993_ip12h ²⁰⁸	dog	NR	m/f	none	local	NA	4	5	20	180
Kuzuya1993_ip24h ²⁰⁸	dog	NR	m/f	none	local	NA	4	5	20	720
Landim2013_healthy ²⁰⁹	rat	NR	m	none	local	NA	3	3	9	3
Landim2013_hyperchol ²⁰⁹	rat	NR	m	hypercholesterolemia	local	NA	3	3	9	3
Lang2006_IPC ²¹⁰	rat	NR	m	none	local	NA	3	5	15	5
Lang2006_RIPC ²¹⁰	rat	NR	m	none	remote	RAO	1	10	10	20
Lange2006 ²¹¹	rabbit	NR	m	none	local	NA	1	5	5	30
Lankford2006 ²¹²	mouse	NR	m	none	local	NA	3	5	15	10
Larsen2007 ²¹³	pig	NR	f	none	local	NA	2	5	10	5
Lasley1995 ²¹⁴	rabbit	NR	m/f	none	local	NA	1	5	5	10
Lazou2006 ²¹⁵	rabbit	NR	m	none	local	NA	1	5	5	10
Lee2000 ²¹⁶	dog	NR	NR	none	local	NA	1	5	5	10
Lee2004_bif1cy ²¹⁷	rabbit	NR	NR	none	local	NA	1	5	5	10
Lee2004_bif3cy ²¹⁷	rabbit	NR	NR	none	local	NA	3	5	15	10
Lee2004_bif5cy ²¹⁷	rabbit	NR	NR	none	local	NA	5	5	25	10
Lee2004_bif7cy ²¹⁷	rabbit	NR	NR	none	local	NA	7	5	35	10
Lee2004_trif1cy ²¹⁷	rabbit	NR	NR	none	local	NA	1	5	5	10

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Lee2004_trif3cy ²¹⁷	rabbit	NR	NR	none	local	NA	3	5	15	10
Lee2004_trif5cy ²¹⁷	rabbit	NR	NR	none	local	NA	5	5	25	10
Li_G1990_01cy ²¹⁸	dog	NR	m	none	local	NA	1	5	5	10
Li_G1990_06cy ²¹⁸	dog	NR	m	none	local	NA	6	5	30	10
Li_G1990_12cy ²¹⁸	dog	NR	m	none	local	NA	12	5	60	10
Li_Q2003 ²¹⁹	mouse	NR	m	none	local	NA	6	4	24	1440
Li_R2009 ²²⁰	rat	NR	m	none	local	NA	3	5	15	5
Li_S2008_IPC ²²¹	rat	NR	NR	none	local	NA	3	5	15	5
Li_S2008_RIPC ²²¹	rat	NR	NR	none	remote	hind limb	9	5	45	1440
Li_S2009_IPC ²²²	rat	NR	NR	none	local	NA	3	5	15	5
Li_S2009_RIPC ²²²	rat	NR	NR	none	remote	hind limb	9	5	45	1440
Li_S2010_IPC ²²³	rat	NR	m	none	local	NA	3	5	15	5
Li_S2010_RIPC ²²³	rat	NR	m	none	remote	hind limb	9	5	45	1440
Li_W2003 ²²⁴	rabbit	NR	m	none	local	NA	4	5	20	1440
Li_X2012a ²²⁵	pig	NR	NR	none	local	NA	3	5	15	5
Li_X2012b ²²⁶	pig	NR	m/f	none	local	NA	3	5	15	5
Li_Y1992a_ip05 ²²⁷	rat	NR	f	none	local	NA	3	3	9	5
Li_Y1992a_ip1h ²²⁷	rat	NR	f	none	local	NA	3	3	9	60
Li_Y1992a_ip2h ²²⁷	rat	NR	f	none	local	NA	3	3	9	120
Li_Y1992a_ip3h ²²⁷	rat	NR	f	none	local	NA	3	3	9	180
Li_Y1992b ²²⁸	rat	NR	f	none	local	NA	3	5	15	5
Li_Y1993a ²²⁹	rat	NR	f	none	local	NA	3	3	9	5
Li_Y1993b ²³⁰	rat	NR	f	none	local	NA	3	3	9	5
Li_Y1994_ip05 ²³¹	rat	NR	f	none	local	NA	3	3	9	5
Li_Y1994_ip1h ²³¹	rat	NR	f	none	local	NA	3	3	9	60
Li_Y1994_ip60ip ²³¹	rat	NR	f	none	local	NA	6	3	18	5
Li_Y1995 ²³²	rat	NR	f	none	local	NA	3	3	9	5
Li_Y2011 ²³³	mouse	NR	m	none	local	NA	3	5	15	1440
Liao2013_convent ²³⁴	mouse	NR	m	none	local	NA	3	5	15	5
Liao2013_lungrec ²³⁴	mouse	NR	m	none	local	NA	3	5	15	5
Liadet2001_mouse ²³⁵	mouse	NR	NR	none	local	NA	4	5	20	10

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Liaudet2001_rat ²³⁵	rat	NR	m	none	local	NA	4	5	20	5
Lie2010 ²³⁶	pig	NR	f	none	local	NA	2	10	20	30
Liem2001_1cy ²³⁷	rat	NR	m	none	local	NA	1	15	15	10
Liem2001_3cy ²³⁷	rat	NR	m	none	local	NA	3	3	9	3
Liem2005_01cyip70 ²³⁸	rat	NR	m	none	local	NA	1	15	15	70
Liem2005_04cyip70 ²³⁸	rat	NR	m	none	local	NA	4	15	60	70
Liem2005_2cy ²³⁸	rat	NR	m	none	local	NA	2	15	30	10
Liem2005_3cy ²³⁸	rat	NR	m	none	local	NA	3	3	9	5
Liem2005_6cy ²³⁸	rat	NR	m	none	local	NA	6	15	90	10
Liem2005_7cy ²³⁸	rat	NR	m	none	local	NA	7	10	70	5
Liem2005_ip010 ²³⁸	rat	NR	m	none	local	NA	1	15	15	10
Liem2005_ip090 ²³⁸	rat	NR	m	none	local	NA	1	15	15	90
Liem2005_ip175 ²³⁸	rat	NR	m	none	local	NA	1	15	15	175
Liem2005_IPC+RIPC ²³⁸	rat	NR	m	none	local+remote	MAO	6	15	90	10
Liem2005_RIPC ²³⁸	rat	NR	m	none	remote	MAO	2	15	30	10
Lim2007_30is ²³⁹	mouse	NR	m/f	none	local	NA	1	5	5	5
Lim2007_45is ²³⁹	mouse	NR	m/f	none	local	NA	1	5	5	5
Lim2010 ²⁴⁰	mouse	NR	m	none	remote	hind limb	3	5	15	5
Liu1993a ²⁴¹	rat	NR	m	diabetes	local	NA	3	5	15	5
Liu1993b ²⁴²	rat	NR	m	none	local	NA	3	5	15	5
Liu1994 ²⁴³	rabbit	NR	m/f	none	local	NA	1	5	5	10
Liu2005 ²⁴⁴	rat	NR	m	none	local	NA	3	5	15	1440
Liu2008 ²⁴⁵	rat	NR	m	none	local	NA	5	4	20	4
LiuG1992a ²⁴⁶	rabbit	NR	m/f	none	local	NA	1	5	5	10
LiuG1992b ²⁴⁷	rabbit	NR	m	none	local	NA	1	5	5	10
LiuY1992_1cy ²⁴⁸	rat	NR	m	none	local	NA	1	5	5	10
LiuY1992_3cy ²⁴⁸	rat	NR	m	none	local	NA	3	5	15	5
Loke1998 ²⁴⁹	dog	NR	m/f	none	local	NA	3	5	15	10
Lott1996 ²⁵⁰	rat	NR	m	none	local	NA	2	5	10	5
Lotz2011 ²⁵¹	rabbit	NR	m	none	remote	RAO	3	10	30	10
Lou2003 ²⁵²	rat	none	m	none	local	NA	3	5	15	5

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Lu2009 ²⁵³	mouse	NR	NR	none	local	NA	3	5	15	5
Lu2011 ²⁵⁴	rat	NR	m	none	local	NA	3	5	15	5
Lu2012_1cy ²⁵⁵	rat	NR	m	none	remote	hind limb	1	5	5	5
Lu2012_3cy ²⁵⁵	rat	NR	m	none	remote	hind limb	3	5	15	5
Luo2004 ²⁵⁶	rat	NR	m	none	local	NA	4	3	12	1440
Manintveld2005 ²⁵⁷	rat	NR	m	none	local	NA	1	15	15	10
Manintveld2011_1cy ²⁵⁸	rat	NR	NR	none	local	NA	1	15	15	10
Manintveld2011_3cy ²⁵⁸	rat	NR	NR	none	local	NA	3	3	9	5
Marber1993 ²⁵⁹	rabbit	yes	NR	none	local	NA	4	5	20	1440
Martin1997 ²⁶⁰	pig	NR	m/f	none	local	NA	1	10	10	10
Matsuda1993 ²⁶¹	dog	NR	m/f	none	local	NA	4	5	20	5
Matsumura2000 ²⁶²	rat	NR	m	none	local	NA	1	3	3	10
McVey1999a ²⁶³	rat	NR	m	none	local	NA	3	3	9	5
McVey1999b ²⁶⁴	dog	NR	NR	none	local	NA	1	5	5	10
Mei1998 ²⁶⁵	dog	NR	NR	none	local	NA	1	5	5	10
Miki1996 ²⁶⁶	rabbit	NR	m	none	local	NA	1	2	2	5
Miki1998a ²⁶⁷	rabbit	NR	m/f	none	local	NA	1	5	5	10
Miki1998b ²⁶⁸	rabbit	NR	m	none	local	NA	1	5	5	5
Miki1999_histo ²⁶⁹	rabbit	none	m/f	none	local	NA	4	5	20	1440
Miki1999_TTC ²⁶⁹	rabbit	none	m/f	none	local	NA	4	5	20	1440
Miller1999_2cy ²⁷⁰	mouse	NR	NR	none	local	NA	3	5	15	5
Miller1999_3cy ²⁷⁰	mouse	NR	NR	none	local	NA	2	5	10	5
Minamino1996_ip005 ²⁷¹	dog	NR	m/f	none	local	NA	4	5	20	5
Minamino1996_ip030 ²⁷¹	dog	NR	m/f	none	local	NA	4	5	20	30
Minamino1996_ip060 ²⁷¹	dog	NR	m/f	none	local	NA	4	5	20	60
Minamino1996_ip120 ²⁷¹	dog	NR	m/f	none	local	NA	4	5	20	120
Miura1991_1cy ²⁷²	rabbit	NR	m	none	local	NA	1	5	5	5
Miura1991_2cy ²⁷²	rabbit	NR	m	none	local	NA	2	5	10	5
Miura1991_2ip ²⁷²	rabbit	NR	m	none	local	NA	2	2	4	5
Miura1992 ²⁷³	rabbit	NR	m	none	local	NA	1	2	2	5
Miura1998_1cy ²⁷⁴	rabbit	NR	m	none	local	NA	1	5	5	5

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Miura1998_2cy ²⁷⁴	rabbit	NR	m	none	local	NA	2	5	10	5
Mizumura1995 ²⁷⁵	dog	NR	m/f	none	local	NA	1	5	5	10
Mizumura1996_2.5ip ²⁷⁶	dog	NR	m/f	none	local	NA	1	3	3	10
Mizumura1996_5ip ²⁷⁶	dog	NR	m/f	none	local	NA	1	5	5	10
Mizumura1997_2.5ip ²⁷⁷	dog	NR	m/f	none	local	NA	1	3	3	10
Mizumura1997_5ip ²⁷⁷	dog	NR	m/f	none	local	NA	1	5	5	10
Morgan1999 ²⁷⁸	rabbit	NR	NR	none	local	NA	3	5	15	120
Mortensen2006 ²⁷⁹	pig	none	NR	none	local	NA	2	10	20	30
Mullenheim2001a ²⁸⁰	rabbit	NR	m	none	local	NA	1	5	5	10
Mullenheim2001b ²⁸¹	rabbit	NR	m	none	local	NA	1	5	5	1440
Mullenheim2001c_ip10 ²⁸²	rabbit	NR	m	none	local	NA	1	5	5	10
Mullenheim2001c_ip24h ²⁸²	rabbit	NR	m	none	local	NA	1	5	5	1440
Mullenheim2001c_ip24hip ²⁸²	rabbit	NR	m	none	local	NA	2	5	10	10
Mullenheim2003_ip24h ²⁸³	rabbit	none	m	none	local	NA	1	5	5	1440
Mullenheim2003_ip24hip ²⁸³	rabbit	none	m	none	local	NA	2	5	10	10
Munch-Ellingsen1997 ²⁸⁴	rabbit	NR	m/f	none	local	NA	1	5	5	10
Munch-Ellingsen1998 ²⁸⁵	rabbit	NR	m/f	none	local	NA	1	5	5	10
Murry1986_3his ²⁸⁶	dog	NR	m/f	none	local	NA	4	5	20	5
Murry1986_40is ²⁸⁶	dog	NR	m/f	none	local	NA	4	5	20	5
Murry1991_ip120 ²⁸⁷	dog	NR	m/f	none	local	NA	1	15	15	120
Murry1991_ip5 ²⁸⁷	dog	NR	m/f	none	local	NA	1	15	15	5
Nadtochiy2009 ²⁸⁸	mouse	NR	m	none	local	NA	3	5	15	5
Nakae2000_2.5ip ²⁸⁹	rabbit	NR	m	none	local	NA	1	3	3	20
Nakae2000_5ip ²⁸⁹	rabbit	NR	m	none	local	NA	1	5	5	20
Nakano1997_3ip ²⁹⁰	rabbit	NR	m	none	local	NA	1	3	3	5
Nakano1997_5ip ²⁹⁰	rabbit	NR	m	none	local	NA	1	5	5	5
Naumenko2010 ²⁹¹	rat	NR	m	none	local	NA	3	3	9	3
Nawada1997 ²⁹²	rabbit	NR	f	none	local	NA	1	5	5	10
Neckar2002_2cy ²⁹³	rat	NR	m	none	local	NA	2	5	10	5
Neckar2002_5cy ²⁹³	rat	NR	m	none	local	NA	5	5	25	5
Nieszner2002_diabetic ²⁹⁴	rabbit	NR	m	diabetes	local	NA	3	2	6	2

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Nieszner2002_healthy ²⁹⁴	rabbit	NR	m	none	local	NA	3	2	6	2
Nishihara2006 ²⁹⁵	rat	NR	m	none	local	NA	1	5	5	5
Nithipatikom2006a ²⁹⁶	dog	NR	m/f	none	local	NA	1	5	5	10
Nithipatikom2006b ²⁹⁷	dog	NR	m/f	none	local	NA	1	5	5	10
Node1997 ²⁹⁸	dog	NR	m/f	none	local	NA	4	5	20	5
Nozawa1999 ²⁹⁹	rabbit	NR	NR	none	local	NA	1	2	2	5
Nozawa2003_ip20 ³⁰⁰	rat	NR	m	none	local	NA	2	5	10	20
Nozawa2003_ip5 ³⁰⁰	rat	NR	m	none	local	NA	2	5	10	5
Okamura1999 ³⁰¹	rat	NR	m	none	local	NA	3	3	9	3
Okubo2000 ³⁰²	rabbit	NR	m	none	local	NA	4	5	20	1440
Okubo2004a ³⁰³	rabbit	NR	m	none	local	NA	4	5	20	10
Okubo2004b_ip10 ³⁰⁴	rabbit	NR	m	none	local	NA	4	5	20	10
Okubo2004b_ip24h ³⁰⁴	rabbit	NR	m	none	local	NA	4	5	20	1440
Ovize1992_60is ³⁰⁵	dog	yes	m/f	none	local	NA	4	3	12	5
Ovize1992_90is ³⁰⁵	dog	yes	m/f	none	local	NA	4	3	12	5
Ovize1995_05ip ³⁰⁶	pig	NR	m/f	none	local	NA	1	5	5	10
Ovize1995_10ip ³⁰⁶	pig	NR	m/f	none	local	NA	1	10	10	10
Pagel2007 ³⁰⁷	rabbit	NR	m	none	local	NA	3	5	15	5
Patel2001 ³⁰⁸	rat	NR	m	none	local	NA	1	5	5	5
Patel2002_1cy ³⁰⁹	rat	NR	m	none	local	NA	1	15	15	5
Patel2002_3cy ³⁰⁹	rat	NR	m	none	local	NA	3	5	15	5
Patel2005 ³¹⁰	rat	NR	m	none	local	NA	3	5	15	1440
Peart2003 ³¹¹	dog	NR	NR	none	local	NA	1	5	5	10
Pell1998 ³¹²	rabbit	yes	m	none	remote	RAO	1	10	10	10
Perricone2013 ³¹³	mouse	NR	m	none	local	NA	3	5	15	5
Petrtschev2006_IPC ³¹⁴	rat	NR	NR	none	local	NA	4	3	12	6
Petrtschev2006_RIPC ³¹⁴	rat	NR	NR	none	remote	MAO	1	20	20	15
Ping1999 ³¹⁵	rabbit	NR	NR	none	local	NA	6	4	24	1440
Ping2002 ³¹⁶	mouse	NR	NR	none	local	NA	6	4	24	1440
Piot1997 ³¹⁷	rat	NR	f	none	local	NA	5	5	25	5
Poulsen2014 ³¹⁸	pig	NR	f	none	local	NA	2	10	20	30

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Przyklenk1993 ³¹⁹	dog	yes	NR	none	remote	LCX	4	5	20	5
Przyklenk1995 ³²⁰	dog	NR	NR	none	local	NA	4	5	20	5
Przyklenk1996 ³²¹	dog	NR	NR	none	local	NA	4	5	20	5
Przyklenk1997 ³²²	dog	NR	NR	none	local	NA	1	10	10	30
Przyklenk2001_adult ³²³	rabbit	NR	NR	none	local	NA	1	5	5	10
Przyklenk2001_middle ³²³	rabbit	NR	NR	middle-age	local	NA	1	5	5	10
Przyklenk2001_old ³²³	rabbit	NR	NR	senescence	local	NA	1	5	5	10
Przyklenk2003_adult ³²⁴	rabbit	NR	m/f	none	local	NA	1	5	5	10
Przyklenk2003_old ³²⁴	rabbit	NR	m/f	senescence	local	NA	1	5	5	10
Qian1996 ³²⁵	rat	NR	NR	none	local	NA	1	5	5	5
Qian1999_1cy ³²⁶	rat	NR	m	none	local	NA	1	5	5	10
Qian1999_1cy24h ³²⁶	rat	NR	m	none	local	NA	1	5	5	1440
Qian1999_2cy24h ³²⁶	rat	NR	m	none	local	NA	2	5	10	1440
Qian1999_3cy ³²⁶	rat	NR	m	none	local	NA	3	5	15	10
Qian1999_3cy24h ³²⁶	rat	NR	m	none	local	NA	3	5	15	1440
Qian1999_3cy48h ³²⁶	rat	NR	m	none	local	NA	3	5	15	2880
Qiu1997a ³²⁷	rabbit	NR	m	none	local	NA	6	4	24	1440
Qiu1997b_25cy ³²⁸	pig	NR	m/f	none	local	NA	25	2	50	1440
Qiu1997b_ip24h ³²⁸	pig	NR	m/f	none	local	NA	10	2	20	1440
Qiu1997b_ip25 ³²⁸	pig	NR	m/f	none	local	NA	10	2	20	25
Rajesh2003_ip10 ³²⁹	rat	NR	m	cardiac hypertrophy	local	NA	4	3	12	10
Rajesh2003_ip24h ³²⁹	rat	NR	m	cardiac hypertrophy	local	NA	4	3	12	1440
Rajesh2003_ip5h ³²⁹	rat	NR	m	cardiac hypertrophy	local	NA	4	3	12	300
Rajesh2004_healthy ³³⁰	rat	NR	m	none	local	NA	4	3	12	10
Rajesh2004_hypertri ³³⁰	rat	NR	m	cardiac hypertrophy	local	NA	4	3	12	10
Raphael2005 ³³¹	rabbit	NR	NR	none	local	NA	1	5	5	10
Redel2009_3cy ³³²	mouse	NR	m	none	local	NA	3	5	15	40
Redel2009_6cy ³³²	mouse	NR	m	none	local	NA	6	5	30	40
Reffelman2003 ³³³	rabbit	NR	m	none	local	NA	1	5	5	10
Ren2004 ³³⁴	mouse	NR	m/f	none	local	NA	6	4	24	1440
Richard1993 ³³⁵	rat	NR	m	none	local	NA	3	5	15	5

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Richard1994 ³³⁶	rat	NR	m	none	local	NA	3	5	15	5
Rioufol1997 ³³⁷	pig	NR	NR	none	local	NA	1	10	10	10
Rivo2006 ³³⁸	rabbit	NR	NR	none	local	NA	1	5	5	10
Roesner2007 ³³⁹	pig	yes	m	none	local	NA	1	10	10	15
Roesner2010 ³⁴⁰	pig	yes	m	none	local	NA	1	10	10	15
Rohmann1994 ³⁴¹	pig	NR	m/f	none	local	NA	1	10	10	15
Sack1993_ip30 ³⁴²	pig	NR	m	none	local	NA	2	10	20	30
Sack1993_ip4dip ³⁴²	pig	NR	m	none	local	NA	4	10	40	30
Sack1993_ip60 ³⁴²	pig	NR	m	none	local	NA	2	10	20	60
Sack1993_ip60ip ³⁴²	pig	NR	m	none	local	NA	4	10	40	30
Sanada2001a_exp1 ³⁴³	dog	NR	NR	none	local	NA	4	5	20	5
Sanada2001a_exp2 ³⁴³	dog	NR	NR	none	local	NA	4	5	20	5
Sanada2001b ³⁴⁴	dog	NR	NR	none	local	NA	4	5	20	5
Sanada2004 ³⁴⁵	dog	NR	NR	none	local	NA	1	5	5	25
Sandhu1997_3cy ³⁴⁶	rabbit	NR	m/f	none	local	NA	3	5	15	10
Sandhu1997_1stab ³⁴⁶	rabbit	NR	m/f	none	local	NA	1	5	5	10
Sandhu1997_sstab ³⁴⁶	rabbit	NR	m/f	none	local	NA	1	5	5	10
Sanz1995 ³⁴⁷	pig	NR	NR	none	local	NA	2	5	10	5
Sarkar2012 ³⁴⁸	mouse	NR	NR	none	local	NA	2	5	10	5
Sasamori2006 ³⁴⁹	dog	NR	m/f	none	local	NA	4	5	20	5
Sato2007_45is ³⁵⁰	rat	NR	m	none	local	NA	12	2	24	1440
Sato2007_60is ³⁵⁰	rat	NR	m	none	local	NA	12	2	24	1440
Sbarouni2006_healthy ³⁵¹	rabbit	NR	f	none	local	NA	2	5	10	10
Sbarouni2006_ovx ³⁵¹	rabbit	NR	f	ovariectomy	local	NA	2	5	10	10
Schmidt2014 ³⁵²	pig	NR	m/f	none	remote	hind limb	4	5	20	5
Schoemaker2000_IPC ³⁵³	rat	NR	m	none	local	NA	1	15	15	10
Schoemaker2000_RIPC ³⁵³	rat	NR	m	none	remote	MAO	1	15	15	10
Schott1990 ³⁵⁴	pig	NR	m	none	local	NA	1	10	10	30
Schultz1995 ³⁵⁵	rat	NR	m	none	local	NA	3	5	15	5
Schultz1996 ³⁵⁶	rat	NR	m	none	local	NA	3	5	15	5
Schultz1997a ³⁵⁷	rat	NR	NR	none	local	NA	1	5	5	10

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Schultz1997b ³⁵⁸	rat	NR	m	none	local	NA	3	5	15	5
Schultz1997c ³⁵⁹	rat	NR	m	none	local	NA	3	5	15	5
Schultz1997d ³⁶⁰	rat	NR	m	none	local	NA	3	5	15	5
Schultz1998a_1cy ³⁶¹	rat	NR	m	none	local	NA	1	5	5	20
Schultz1998a_3cy ³⁶¹	rat	NR	m	none	local	NA	3	5	15	5
Schultz1998b_exp1 ³⁶²	rat	NR	m	none	local	NA	3	5	15	5
Schultz1998b_exp2 ³⁶²	rat	NR	m	none	local	NA	3	5	15	5
Schultz1998c ³⁶³	rat	NR	m	none	local	NA	3	5	15	5
Schulz1994 ³⁶⁴	pig	NR	m/f	none	local	NA	1	10	10	15
Schwartz1997 ³⁶⁵	dog	none	m/f	none	local	NA	1	5	5	10
Schwartz2001_2cy ³⁶⁶	dog	NR	m/f	none	local	NA	2	10	20	10
Schwartz2001_ip10 ³⁶⁶	dog	NR	m/f	none	local	NA	1	10	10	10
Schwartz2001_ip2h ³⁶⁶	dog	NR	m/f	none	local	NA	1	10	10	120
Schwartz2001_ip3h ³⁶⁶	dog	NR	m/f	none	local	NA	1	10	10	180
Schwartz2001_ip5h ³⁶⁶	dog	NR	m/f	none	local	NA	1	10	10	300
Schwartz2002 ³⁶⁷	pig	NR	m/f	none	local	NA	2	5	10	10
Schwarz1997 ³⁶⁸	pig	NR	m	none	local	NA	2	10	20	30
Schwarz1998_ip24h ³⁶⁹	pig	NR	m	none	local	NA	2	10	20	1440
Schwarz1998_ip30 ³⁶⁹	pig	NR	m	none	local	NA	2	10	20	30
Schwarz1998_ip5h ³⁶⁹	pig	NR	m	none	local	NA	2	10	20	300
Schwarz1998_ip60 ³⁶⁹	pig	NR	m	none	local	NA	2	10	20	60
Schwarz1998_ip90 ³⁶⁹	pig	NR	m	none	local	NA	2	10	20	90
Sebbag1996 ³⁷⁰	dog	yes	m/f	none	local	NA	4	5	20	5
Shahid2008 ³⁷¹	rat	NR	m	none	remote	hind limb	1	15	15	10
Shattock1996 ³⁷²	pig	NR	m	none	local	NA	2	8	16	8
Shekarforoush2011 ³⁷³	rat	NR	m	none	local	NA	1	5	5	NR
Sheldrick1999 ³⁷⁴	rabbit	NR	m	none	local	NA	1	5	5	10
Shen2008 ³⁷⁵	pig	NR	f	none	local	NA	2	10	20	1440
Shen2013 ³⁷⁶	rat	NR	m	none	local	NA	3	7	21	10
Shinmura2000 ³⁷⁷	rabbit	NR	m	none	local	NA	6	4	24	1440
Shinmura2002 ³⁷⁸	rabbit	NR	m	none	local	NA	6	4	24	1440

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Shintani2004 ³⁷⁹	dog	NR	NR	none	local	NA	4	5	20	5
Singh2000 ³⁸⁰	rat	NR	m/f	none	local	NA	4	5	20	1440
Singh2004 ³⁸¹	rat	NR	m/f	none	remote	RAO	4	5	20	10
Sivarajah2005 ³⁸²	rat	NR	m	none	local	NA	2	5	10	5
Sivarajah2006 ³⁸³	rat	NR	m	none	local	NA	2	5	10	5
Smits1998 ³⁸⁴	pig	NR	m/f	none	local	NA	2	5	10	10
Smul2011 ³⁸⁵	rabbit	NR	m	none	local	NA	1	5	5	30
Speechly-Dick1994a ³⁸⁶	rat	NR	m	none	local	NA	1	5	5	10
Speechly-Dick1994b_healthy ³⁸⁷	rat	NR	m	none	local	NA	1	5	5	10
Speechly-Dick1994b_hypert ³⁸⁷	rat	NR	m	hypertension	local	NA	1	5	5	10
Strohm2000 ³⁸⁸	pig	NR	m	none	local	NA	2	10	20	10
Su2006 ³⁸⁹	rat	NR	m	none	local	NA	2	5	10	5
Suzuki1998_2ip ³⁹⁰	rabbit	NR	m	none	local	NA	1	2	2	5
Suzuki1998_3ip ³⁹⁰	rabbit	NR	m	none	local	NA	1	3	3	5
Takano1998a ³⁹¹	rabbit	NR	m	none	local	NA	6	4	24	1440
Takano1998b ³⁹²	rabbit	NR	m	none	local	NA	6	4	24	1440
Takano2000a ³⁹³	rabbit	NR	m	none	local	NA	6	4	24	1440
Takano2000b ³⁹⁴	rabbit	NR	m	none	local	NA	6	4	24	1440
Takaoka1999_IPC ³⁹⁵	rabbit	NR	m	none	local	NA	1	5	5	20
Takaoka1999_RIPC ³⁹⁵	rabbit	NR	m	none	remote	RAO	1	10	10	20
Takasaki1998 ³⁹⁶	rat	NR	m	none	local	NA	3	5	15	5
Talukder2010_f30is ³⁹⁷	mouse	NR	f	none	local	NA	3	5	15	5
Talukder2010_f60is ³⁹⁷	mouse	NR	f	none	local	NA	3	5	15	5
Talukder2010_m30is ³⁹⁷	mouse	NR	m	none	local	NA	3	5	15	5
Talukder2010_m60is ³⁹⁷	mouse	NR	m	none	local	NA	3	5	15	5
Tanaka1994a_4cy24h ³⁹⁸	rabbit	NR	m	none	local	NA	4	5	20	1440
Tanaka1994a_4cy48h ³⁹⁸	rabbit	NR	m	none	local	NA	4	5	20	2880
Tanaka1994a_ip24h ³⁹⁸	rabbit	NR	m	none	local	NA	1	5	5	1440
Tanaka1994a_ip2h ³⁹⁸	rabbit	NR	m	none	local	NA	1	5	5	120
Tanaka1994a_ip5 ³⁹⁸	rabbit	NR	m	none	local	NA	1	5	5	5
Tanaka1994b ³⁹⁹	rabbit	NR	m	none	local	NA	1	5	5	5

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Tang2004 ⁴⁰⁰	rabbit	NR	m	none	local	NA	6	4	24	1440
Tang2005_exp1 ⁴⁰¹	rabbit	NR	m	none	local	NA	6	4	24	1440
Tang2005_exp2 ⁴⁰¹	rabbit	NR	m	none	local	NA	6	4	24	1440
Tang2005_hypercho ⁴⁰¹	rabbit	NR	m	hypercholesterolemia	local	NA	6	4	24	1440
Tang2006_ip2_30is ⁴⁰²	rat	NR	m	none	local	NA	12	2	24	2
Tang2006_ip2_45is ⁴⁰²	rat	NR	m	none	local	NA	12	2	24	2
Tang2006_ip2_60is ⁴⁰²	rat	NR	m	none	local	NA	12	2	24	2
Tang2006_ip24h_30is ⁴⁰²	rat	NR	m	none	local	NA	12	2	24	1440
Tang2006_ip24h_45is ⁴⁰²	rat	NR	m	none	local	NA	12	2	24	1440
Tang2006_ip24h_60is ⁴⁰²	rat	NR	m	none	local	NA	12	2	24	1440
Tanhehco2000 ⁴⁰³	rabbit	NR	m	none	local	NA	2	5	10	10
Tanno2000_1cy ⁴⁰⁴	rat	NR	m	none	local	NA	1	5	5	5
Tanno2000_2cyexp1 ⁴⁰⁴	rat	NR	m	none	local	NA	2	5	10	5
Tanno2000_2cyexp2 ⁴⁰⁴	rat	NR	m	none	local	NA	2	5	10	5
Tanno2000_2cyexp3 ⁴⁰⁴	rat	NR	m	none	local	NA	2	5	10	5
Tanno2000_2cyexp4 ⁴⁰⁴	rat	NR	m	none	local	NA	2	5	10	5
Thornton1990 ⁴⁰⁵	rabbit	NR	m/f	none	local	NA	2	5	10	10
Thornton1992 ⁴⁰⁶	rabbit	NR	m/f	none	local	NA	2	5	10	10
Thornton1993a ⁴⁰⁷	rabbit	NR	m/f	none	local	NA	1	5	5	10
Thornton1993b ⁴⁰⁸	rabbit	NR	m/f	none	local	NA	1	5	5	10
Thornton1993c ⁴⁰⁹	rabbit	NR	m/f	none	local	NA	2	5	10	10
Tissier2001 ⁴¹⁰	rabbit	NR	m	none	local	NA	6	4	24	1440
Tissier2002_3drep ⁴¹¹	rabbit	NR	m	none	local	NA	6	4	24	1440
Tissier2002_3drep_hist ⁴¹¹	rabbit	NR	m	none	local	NA	6	4	24	1440
Tissier2002_3hrep ⁴¹¹	rabbit	NR	m	none	local	NA	6	4	24	1440
Toller1999 ⁴¹²	dog	NR	m/f	none	local	NA	1	2	2	60
Toombs1993a ⁴¹³	rabbit	NR	m/f	none	local	NA	1	5	5	10
Toufektsian2003 ⁴¹⁴	rat	NR	m	none	local	NA	1	5	5	5
Toyoda2000_30is ⁴¹⁵	sheep	NR	m/f	none	local	NA	1	5	5	5
Toyoda2000_45is ⁴¹⁵	sheep	NR	m/f	none	local	NA	1	5	5	5
Toyoda2000_60is ⁴¹⁵	sheep	NR	m/f	none	local	NA	1	5	5	5

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Tranter2010 ⁴¹⁶	mouse	NR	m/f	none	local	NA	6	4	24	1440
Tsovolas2008 ⁴¹⁷	rabbit	NR	m	none	local	NA	2	5	10	10
Tsuchida1992 ⁴¹⁸	rabbit	NR	m	none	local	NA	1	5	5	5
Tsuchida1994a ⁴¹⁹	rabbit	NR	m/f	none	local	NA	1	5	5	10
Tsuchida1994b ⁴²⁰	rabbit	NR	m/f	none	local	NA	1	5	5	120
Tsuchida1998_20is ⁴²¹	rat	NR	m	none	local	NA	2	5	10	5
Tsuchida1998_30is ⁴²¹	rat	NR	m	none	local	NA	2	5	10	5
Tsuchida1998_40is ⁴²¹	rat	NR	m	none	local	NA	2	5	10	5
Turan2008 ⁴²²	rat	NR	m	none	local	NA	1	5	5	10
Ueda1999_healthy ⁴²³	rabbit	NR	NR	none	local	NA	1	5	5	10
Ueda1999_hyperchol ⁴²³	rabbit	NR	NR	hypercholesterolemia	local	NA	1	5	5	10
Uematsu1998 ⁴²⁴	sheep	NR	m/f	none	local	NA	1	5	5	5
Valtchanova2004_ip24h ⁴²⁵	rat	NR	m	none	local	NA	3	5	15	1440
Valtchanova2004_ip5 ⁴²⁵	rat	NR	m	none	local	NA	3	5	15	5
Valtchanova-Matchouganska2003 ⁴²⁶	rat	NR	m	none	local	NA	3	5	15	5
VandenDoel1998_030is ⁴²⁷	rat	NR	m	none	local	NA	1	15	15	10
VandenDoel1998_045is ⁴²⁷	rat	NR	m	none	local	NA	1	15	15	10
VandenDoel1998_060is ⁴²⁷	rat	NR	m	none	local	NA	1	15	15	10
VandenDoel1998_120is ⁴²⁷	rat	NR	m	none	local	NA	1	15	15	10
VanderHeide1994 ⁴²⁸	dog	yes	m/f	none	local	NA	4	5	20	5
VanWinkle1994b ⁴²⁹	pig	yes	NR	none	local	NA	2	10	20	10
VanWylen1994 ⁴³⁰	dog	yes	m/f	none	local	NA	2	5	10	10
Vetterlein2006 ⁴³¹	rat	NR	m	none	local	NA	3	5	15	10
Vincent2012 ⁴³²	mouse	NR	m	none	local	NA	3	1	3	10
Virag2013 ⁴³³	mouse	NR	f	none	local	NA	3	5	15	5
Vladic2011_mouse ⁴³⁴	mouse	NR	m	hyperglycaemia	local	NA	4	5	20	5
Vladic2011_rbhealthy ⁴³⁴	rabbit	NR	m	hyperglycaemia	local	NA	1	5	5	15
Vladic2011_rbhypergly ⁴³⁴	rabbit	NR	m	hyperglycaemia	local	NA	1	5	5	15
Vogt1998_ip30 ⁴³⁵	pig	NR	m	none	local	NA	2	10	20	30
Vogt1998_ip60 ⁴³⁵	pig	NR	m	none	local	NA	2	10	20	60
Vogt1998_ip60ip ⁴³⁵	pig	NR	m	none	local	NA	4	10	40	30

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Vogt2001_1cy ⁴³⁶	pig	NR	m	none	local	NA	1	10	10	30
Vogt2001_2cy ⁴³⁶	pig	NR	m	none	local	NA	2	10	20	30
Wall1994 ⁴³⁷	rabbit	NR	m/f	none	local	NA	1	5	5	10
Walsh1994 ⁴³⁸	rabbit	NR	NR	none	local	NA	1	5	5	10
Wang2001 ⁴³⁹	rat	NR	m	none	remote	MAO	1	30	30	1440
Wang2002 ⁴⁴⁰	rat	NR	m	none	remote	MAO	1	25	25	15
Wang2009 ⁴⁴¹	rat	NR	m	none	remote	hind limb	3	5	15	5
WangS2004 ⁴⁴²	sheep	NR	m	none	local	NA	3	5	15	10
WangY2004_ip24h ⁴⁴³	rabbit	NR	m	none	local	NA	6	4	24	1440
WangY2004_ip72h ⁴⁴³	rabbit	NR	m	none	local	NA	6	4	24	4320
Watanabe2006 ⁴⁴⁴	rat	NR	m	coronary stenosis	local	NA	2	5	10	5
Weber2005 ⁴⁴⁵	rat	NR	m	none	local	NA	3	5	15	5
Weber2008 ⁴⁴⁶	rat	NR	m	none	local	NA	1	5	5	1440
Weinbrenner2002_IPC ⁴⁴⁷	rat	NR	m	none	local	NA	3	5	15	5
Weinbrenner2002_RIPC05 ⁴⁴⁷	rat	NR	m	none	remote	IAO	1	5	5	10
Weinbrenner2002_RIPC10 ⁴⁴⁷	rat	NR	m	none	remote	IAO	1	10	10	10
Weinbrenner2002_RIPC15 ⁴⁴⁷	rat	NR	m	none	remote	IAO	1	15	15	10
Weinbrenner2004_1cy ⁴⁴⁸	rat	NR	m	none	local	NA	1	5	5	5
Weinbrenner2004_3cy ⁴⁴⁸	rat	NR	m	none	local	NA	3	5	15	5
Weinbrenner2004_RIPC ⁴⁴⁸	rat	NR	m	none	remote	IAO	1	15	15	10
Wolfe1993_ip30 ⁴⁴⁹	rat	NR	m	none	local	NA	4	5	20	30
Wolfe1993_ip360 ⁴⁴⁹	rat	NR	m	none	local	NA	4	5	20	360
Wolfe1993_ip5 ⁴⁴⁹	rat	NR	m	none	local	NA	4	5	20	5
Wolfe1993_ip60 ⁴⁴⁹	rat	NR	m	none	local	NA	4	5	20	60
Wolfrum2002 ⁴⁵⁰	rat	NR	m	none	remote	MAO	1	15	15	15
Wolfrum2005 ⁴⁵¹	rat	NR	m	none	remote	MAO	1	15	15	15
Wong2010 ⁴⁵²	rat	NR	m	none	local	NA	3	5	15	5
Wong2012_IPC1 ⁴⁵³	rat	NR	m	none	local	NA	3	5	15	5
Wong2012_IPC2 ⁴⁵³	rat	NR	m	none	local	NA	3	5	15	5
Wong2012_RIPC1 ⁴⁵³	rat	NR	m	none	remote	hind limb	3	5	15	5
Wong2012_RIPC2 ⁴⁵³	rat	NR	m	none	remote	hind limb	3	5	15	5

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Wu2001 ⁴⁵⁴	rabbit	NR	m	none	local	NA	1	5	5	5
Wu2008a ⁴⁵⁵	rat	NR	m	diabetes	local	NA	3	5	15	5
Wu2008b_IPC ⁴⁵⁶	rat	NR	m	none	local	NA	3	5	15	5
Wu2008b_RIPC ⁴⁵⁶	rat	NR	m	none	remote	hind limb	9	5	45	1440
Wu2009 ⁴⁵⁷	rat	NR	m	diabetes	local	NA	3	5	15	5
Wu2011_IPC ⁴⁵⁸	rat	NR	m	none	local	NA	3	5	15	5
Wu2011_RIPC ⁴⁵⁸	rat	NR	m	none	remote	hind limb	9	5	45	1440
Wu2013 ⁴⁵⁹	rabbit	NR	NR	none	local	NA	2	10	20	10
Xiang2011_early ⁴⁶⁰	mouse	NR	m	none	local	NA	3	4	12	4
Xiang2011_late24hR ⁴⁶⁰	mouse	NR	m	none	local	NA	3	4	12	1440
Xiang2011_late40R ⁴⁶⁰	mouse	NR	m	none	local	NA	3	4	12	1440
Xiao2001_ip24h ⁴⁶¹	rat	NR	m	none	local	NA	6	4	24	1440
Xiao2001_ip48h ⁴⁶¹	rat	NR	m	none	local	NA	6	4	24	2880
Xiao2001_ip72h ⁴⁶¹	rat	NR	m	none	local	NA	6	4	24	4320
Xiong2011 ⁴⁶²	rat	NR	m	none	local	NA	3	5	15	5
Xu2001 ⁴⁶³	rabbit	NR	m/f	none	local	NA	3	5	15	20
Xu2002 ⁴⁶⁴	rabbit	NR	m/f	none	local	NA	1	5	5	10
Xu2006 ⁴⁶⁵	rabbit	NR	m/f	none	local	NA	1	5	5	10
Xu2010 ⁴⁶⁶	rat	NR	m	none	local	NA	3	5	15	1440
Xu2013 ⁴⁶⁷	rabbit	NR	m/f	none	local	NA	1	5	5	10
Xuan2007 ⁴⁶⁸	mouse	NR	NR	none	local	NA	6	4	24	4
Yada2006 ⁴⁶⁹	dog	yes	m/f	none	local	NA	4	5	20	5
Yamada2002_2ip ⁴⁷⁰	rabbit	NR	m	none	local	NA	1	2	2	10
Yamada2002_5ip ⁴⁷⁰	rabbit	NR	m	none	local	NA	1	5	5	10
Yamasaki1997_05ip ⁴⁷¹	rabbit	NR	m	none	local	NA	1	5	5	5
Yamasaki1997_10ip ⁴⁷¹	rabbit	NR	m	none	local	NA	1	10	10	5
Yamasaki1997_15ip ⁴⁷¹	rabbit	NR	m	none	local	NA	1	15	15	5
Yamasaki2000_45is ⁴⁷²	rabbit	NR	m	none	local	NA	1	5	5	5
Yamasaki2000_50is ⁴⁷²	rabbit	NR	m	none	local	NA	1	5	5	5
Yamasaki2000_ip005 ⁴⁷²	rabbit	NR	m	none	local	NA	1	5	5	5
Yamasaki2000_ip040 ⁴⁷²	rabbit	NR	m	none	local	NA	1	5	5	40

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comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
Yamasaki2000_ip120 ⁴⁷²	rabbit	NR	m	none	local	NA	1	5	5	120
Yamashita1998_ip10 ⁴⁷³	rat	NR	m	none	local	NA	4	3	12	10
Yamashita1998_ip24h ⁴⁷³	rat	NR	m	none	local	NA	4	3	12	1440
Yamashita1998_ip3h ⁴⁷³	rat	NR	m	none	local	NA	4	3	12	180
Yamashita2000 ⁴⁷⁴	rat	NR	m	none	local	NA	4	3	12	1440
Yang1993_1cy ⁴⁷⁵	rabbit	NR	m/f	none	local	NA	1	5	5	120
Yang1993_2cy ⁴⁷⁵	rabbit	NR	m/f	none	local	NA	2	5	10	10
Yang1996 ⁴⁷⁶	rabbit	none	NR	none	local	NA	4	5	20	1440
Yang2006 ⁴⁷⁷	pig	NR	NR	none	local	NA	3	10	30	5
Yang2010 ⁴⁷⁸	macaque	NR	m	none	local	NA	2	10	20	10
Yang2011 ⁴⁷⁹	rat	NR	m	none	local	NA	4	3	12	5
YangX2013 ⁴⁸⁰	rat	NR	m	none	local	NA	3	5	15	5
YangZ2013 ⁴⁸¹	mouse	NR	NR	none	local	NA	2	5	10	5
Yao1993a ⁴⁸²	dog	NR	m/f	none	local	NA	1	10	10	10
Yao1993b ⁴⁸³	dog	NR	m/f	none	local	NA	1	10	10	10
Yao1994a_ip10 ⁴⁸⁴	dog	NR	m/f	none	local	NA	1	10	10	10
Yao1994a_ip60 ⁴⁸⁴	dog	NR	m/f	none	local	NA	1	10	10	60
Yao1994b_10ip ⁴⁸⁵	dog	NR	m/f	none	local	NA	1	10	10	10
Yao1994b_3ip ⁴⁸⁵	dog	NR	m/f	none	local	NA	1	3	3	10
Yao1997 ⁴⁸⁶	dog	NR	m/f	none	local	NA	1	10	10	60
Yellon1992 ⁴⁸⁷	rat	NR	m	none	local	NA	1	5	5	10
Yorozuya2004_1cy ⁴⁸⁸	rabbit	NR	m	none	local	NA	1	5	5	5
Yorozuya2004_4cy ⁴⁸⁸	rabbit	NR	m	none	local	NA	4	5	20	5
Ytrehus1994 ⁴⁸⁹	rabbit	NR	m/f	none	local	NA	1	5	5	10
Yu2007 ⁴⁹⁰	rat	NR	m	none	local	NA	3	5	15	1440
Yu2010 ⁴⁹¹	rat	NR	NR	none	local	NA	12	5	60	NR
Yu2011 ⁴⁹²	rat	NR	m	none	local	NA	2	5	10	5
Zacharowski2007 ⁴⁹³	rat	none	m	none	local	NA	3	2	6	10
Zhang2004 ⁴⁹⁴	rat	NR	m	none	local	NA	3	5	15	5
Zhang2010 ⁴⁹⁵	rat	NR	f	none	local	NA	2	5	10	5
ZhangS2006 ⁴⁹⁶	rat	NR	m	none	local	NA	3	5	15	5

Supplemental table A - study and comparison characteristics - page 26 of 26

comparison	species	opioids pre-IPC	sex (m/f)	condition / comorbidity	site of IPC	remote organ	IPC # ischemic cycli	IPC ischemic cycle (min)	IPC total ischemia (min)	IPC to IRI delay (min)
ZhangX2006 ⁴⁹⁷	rabbit	NR	m/f	none	local	NA	3	5	15	5
Zhao2003 ⁴⁹⁸	dog	yes	m/f	none	local	NA	1	5	5	10
Zhao2012_ip24h ⁴⁹⁹	rat	NR	m	none	local	NA	3	5	15	1440
Zhao2012_ip5 ⁴⁹⁹	rat	NR	m	none	local	NA	3	5	15	5
Zhu2007 ⁵⁰⁰	mouse	NR	m	none	local	NA	3	5	15	15
Zhu2009_IPC ⁵⁰¹	rat	NR	NR	diabetes	local	NA	3	5	15	5
Zhu2009_RIPC ⁵⁰¹	rat	NR	NR	diabetes	remote	hind limb	9	5	45	5
Zhu2011_IPC ⁵⁰²	rat	NR	m	diabetes	local	NA	3	5	15	5
Zhu2011_RIPC ⁵⁰²	rat	NR	m	diabetes	remote	hind limb	9	5	45	5
Zhu2013 ⁵⁰³	rat	NR	m	none	remote	hind limb	3	5	15	5

Meta-analysis includes data from 785 independent comparisons identified from 503 studies. Multiple comparisons from a single study are indicated by an underscore followed by a comparison code. IPC = ischemic preconditioning, m = male, f = female, IRI = ischemia-reperfusion injury, NR = not reported, NA = not applicable, IAO = infrarenal aorta occlusion, RAO = renal artery occlusion, MAO = mesenteric artery occlusion, LCX = left circumflex coronary artery occlusion.

Supplemental Table B - study quality and risk of bias - page 1 of 12

study	reporting - randomization	reporting - blinding	reporting - power calculation	bias - random group allocation	bias - groups similar at baseline	bias - blinded group allocation	bias - random housing	bias - blind intervention	bias - random outcome assessment	bias - blind outcome assessment	bias - reporting of drop-outs	bias - other
Alcindor2004 ¹	Y	N	N	?	?	?	?	?	?	?	L	L
Alizadeh2011 ²	N	N	N	?	L	?	?	?	?	?	H	L
Alkhulaifi1993 ³	Y	N	N	?	?	?	?	?	?	?	?	L
Amour2009 ⁴	Y	N	N	?	L	?	?	?	?	?	H	H
Andreadou2004 ⁵	Y	N	N	?	?	?	?	?	?	?	L	L
Andreadou2006 ⁶	Y	N	N	?	?	?	?	?	?	?	L	L
Andreadou2011 ⁷	Y	N	N	?	?	?	?	?	?	?	?	L
Aouam2005 ⁸	Y	N	N	?	L	?	?	?	?	?	H	H
Argaud2004 ⁹	Y	N	N	?	L	?	?	?	?	?	?	L
Argaud2005a ¹⁰	Y	N	N	?	L	?	?	?	?	?	?	L
Argaud2005b ¹¹	Y	Y	N	?	L	?	?	?	?	?	L	L
Argaud2005c ¹²	N	N	N	?	L	?	?	?	?	?	L	L
Argaud2008 ¹³	N	N	N	?	?	?	?	?	?	?	?	L
Auchampach1992 ¹⁴	N	N	N	?	?	?	?	?	?	?	?	L
Auchampach1993 ¹⁵	Y	N	N	?	?	?	?	?	?	?	L	L
Auchampach2004 ¹⁶	Y	N	N	?	?	?	?	?	?	?	H	L
Aye1999 ¹⁷	N	N	N	?	L	?	?	?	?	?	?	L
Baines1997 ¹⁸	N	N	N	?	?	?	?	?	?	?	?	L
Baines1999 ¹⁹	N	N	N	?	?	?	?	?	?	?	?	L
Barbosa1996 ²⁰	Y	N	N	?	L	?	?	?	?	?	?	L
Basalay2012 ²¹	N	N	N	?	L	?	?	?	?	?	H	L
Baumert2007 ²²	Y	Y	Y	?	?	?	?	?	?	L	L	L
Baxter1994 ²³	Y	N	N	?	?	?	?	?	?	?	L	L
Baxter1995 ²⁴	N	N	N	?	?	?	?	?	?	?	L	L
Baxter1997 ²⁵	Y	Y	N	?	?	?	?	?	?	?	?	L
Belosjorow1999 ²⁶	N	N	N	?	?	?	?	?	?	?	L	L
Belosjorow2003 ²⁷	N	N	N	?	?	?	?	?	?	?	L	L
Bencsik2010 ²⁸	N	N	N	?	?	?	?	?	?	?	?	L
Bernardo1999 ²⁹	Y	N	N	?	H	?	?	?	?	?	?	L
Bibli2013 ³⁰	Y	N	N	?	L	?	?	?	?	?	L	L
Blokhin2008a ³¹	N	N	N	?	?	?	?	?	?	?	L	L
Blokhin2008b ³²	N	N	N	?	?	?	?	?	?	?	H	L
Boengler2007 ³³	N	N	N	?	H	?	?	?	?	?	H	L
Brandenburger2012 ³⁴	Y	N	N	?	?	?	?	?	?	?	?	L
Bukhari1995 ³⁵	Y	N	N	?	?	?	?	?	?	?	?	L
Burckhardt1995 ³⁶	Y	N	N	?	?	?	?	?	?	?	L	L
Burns1996 ³⁷	N	N	N	?	?	?	?	?	?	?	L	L
Cai2008 ³⁸	N	N	N	?	L	?	?	?	?	?	?	L
Cai2013 ³⁹	N	N	N	?	?	?	?	?	?	?	?	L
Canyon2005 ⁴⁰	Y	N	N	?	?	?	?	?	?	?	H	L
Cason1997 ⁴¹	Y	N	N	L	?	?	?	?	?	?	L	L
Chazov2001 ⁴²	N	N	N	?	?	?	?	?	?	?	?	L
Chen1997 ⁴³	N	N	N	?	?	?	?	?	?	?	?	L
Chen2005 ⁴⁴	Y	Y	N	?	?	?	?	?	?	L	L	L
Chen2008 ⁴⁵	Y	N	N	?	L	?	?	?	?	?	?	L

Supplemental Table B - study quality and risk of bias - page 2 of 12

study	reporting - randomization	reporting - blinding	reporting - power calculation	bias - random group allocation	bias - groups similar at baseline	bias - blinded group allocation	bias - random housing	bias - blind intervention	bias - random outcome assessment	bias - blind outcome assessment	bias - reporting of drop-outs	bias - other
Cheng2009 ⁴⁶	Y	N	N	?	?	?	?	?	?	?	?	L
Cheng2010a ⁴⁷	N	N	N	?	?	?	?	?	?	?	?	L
Cheng2010b ⁴⁸	N	N	N	?	?	?	?	?	?	?	?	L
Chiari2002 ⁴⁹	N	N	N	?	?	?	?	?	?	?	L	L
Chien1996 ⁵⁰	Y	N	N	?	L	?	?	?	?	?	L	L
Chien1999 ⁵¹	Y	N	N	?	L	?	?	?	?	?	H	L
Cohen1991 ⁵²	Y	N	N	?	?	?	?	?	?	?	L	L
Cohen1994 ⁵³	Y	N	N	H	?	?	?	?	?	?	L	L
Cohen1999 ⁵⁴	Y	N	N	?	?	?	?	?	?	?	L	L
Cohen2000 ⁵⁵	Y	Y	N	?	?	?	?	?	?	?	L	L
Colantonio2004 ⁵⁶	Y	Y	N	?	?	?	?	?	?	?	?	L
Dai2003 ⁵⁷	Y	N	N	?	L	?	?	?	?	?	L	L
Dai2009 ⁵⁸	Y	N	N	?	L	?	?	?	?	?	L	L
Dairaku2002 ⁵⁹	N	N	N	?	?	?	?	?	?	?	?	L
Daleau2001 ⁶⁰	N	N	N	?	L	?	?	?	?	?	?	L
Das2006 ⁶¹	N	N	N	?	L	?	?	?	?	?	?	L
Das2007 ⁶²	N	N	N	?	L	?	?	?	?	?	?	L
Das2012 ⁶³	Y	Y	N	?	L	?	?	?	L	L	L	L
Dawn2002 ⁶⁴	N	N	N	?	?	?	?	?	?	?	L	L
Dawn2004a ⁶⁵	N	N	N	?	?	?	?	?	?	?	L	L
Dawn2004b ⁶⁶	N	N	N	?	?	?	?	?	?	?	H	L
Demiryurek2005a ⁶⁷	N	N	N	?	L	?	?	?	?	?	L	L
Demiryurek2005b ⁶⁸	N	N	N	?	L	?	?	?	?	?	?	L
DePaulis2013 ⁶⁹	Y	N	N	?	L	?	?	?	?	?	?	L
Depre2010 ⁷⁰	N	N	N	?	?	?	?	?	?	?	L	L
Deuchar2007 ⁷¹	N	N	N	?	?	?	?	?	?	?	?	L
DeZeeuw2001 ⁷²	N	N	N	?	?	?	?	?	?	?	L	L
Ding2000 ⁷³	N	N	N	?	?	?	?	?	?	?	L	L
Ding2001 ⁷⁴	N	N	N	?	L	?	?	?	?	?	?	L
Dong2004 ⁷⁵	N	N	N	?	?	?	?	?	?	?	?	L
Ebel2003 ⁷⁶	Y	N	N	?	L	?	?	?	?	?	?	L
Ebel2009 ⁷⁷	Y	N	N	?	L	?	?	?	?	?	?	L
Eckle2006 ⁷⁸	N	N	N	?	?	?	?	?	?	?	?	L
Eckle2012 ⁷⁹	N	N	N	?	?	?	?	?	?	?	?	L
Erikson1996 ⁸⁰	Y	N	N	?	H	?	?	?	?	?	L	L
Fang2008 ⁸¹	Y	Y	N	?	?	?	?	?	?	?	?	L
Farhat2001 ⁸²	Y	N	N	?	?	?	?	?	?	?	?	L
Fisher2002 ⁸³	N	N	N	?	?	?	?	?	?	?	?	L
Flack3rd1991 ⁸⁴	N	N	N	?	?	?	?	?	?	?	?	L
Flaherty2008 ⁸⁵	N	N	N	?	L	?	?	?	?	?	H	L
Flynn2005 ⁸⁶	Y	Y	N	?	?	?	?	?	?	?	?	L
Fryer1998 ⁸⁷	Y	N	N	?	L	?	?	?	?	?	?	L
Fryer1999 ⁸⁸	Y	N	N	?	L	?	?	?	?	?	?	L
Fryer2000 ⁸⁹	Y	N	N	?	?	?	?	?	?	?	?	L
Fryer2001a ⁹⁰	N	N	N	?	L	?	?	?	?	?	?	L

Supplemental Table B - study quality and risk of bias - page 3 of 12

study	reporting - randomization	reporting - blinding	reporting - power calculation	bias - random group allocation	bias - groups similar at baseline	bias - blinded group allocation	bias - random housing	bias - blind intervention	bias - random outcome assessment	bias - blind outcome assessment	bias - reporting of drop-outs	bias - other
Fryer2001b ⁹¹	N	N	N	?	L	?	?	?	?	?	?	L
Fryer2001c ⁹²	N	N	N	?	L	?	?	?	?	?	?	L
Fryer2002 ⁹³	Y	N	N	?	L	?	?	?	?	?	?	L
Fukuma2000 ⁹⁴	N	N	N	?	L	?	?	?	?	?	?	L
Galagudza2007a ⁹⁵	N	N	N	?	L	?	?	?	?	?	L	L
Galagudza2007b ⁹⁶	N	N	N	?	?	?	?	?	?	?	L	L
Galagudza2009 ⁹⁷	N	N	N	?	?	?	?	?	?	?	L	L
Gao2000 ⁹⁸	N	Y	N	?	?	?	?	?	?	L	?	L
Gao2003 ⁹⁹	Y	N	N	?	?	?	?	?	?	?	?	L
Gao2012 ¹⁰⁰	Y	N	N	?	?	?	?	?	?	?	L	L
Ge2011 ¹⁰¹	Y	N	N	?	?	?	?	?	?	?	?	L
Gerczuk2012 ¹⁰²	Y	N	N	?	L	?	?	?	?	?	L	L
Gho1996 ¹⁰³	N	N	N	?	?	?	?	?	?	?	L	L
Gomez2011 ¹⁰⁴	Y	N	N	?	?	?	?	?	?	?	?	L
Gomoll1996 ¹⁰⁵	N	N	N	?	L	?	?	?	?	?	?	L
Goto1993 ¹⁰⁶	Y	N	N	?	L	?	?	?	?	?	L	L
Gourine2005 ¹⁰⁷	Y	N	N	?	L	?	?	?	?	?	L	L
Gozal2005 ¹⁰⁸	Y	N	N	L	?	?	?	?	?	?	?	L
Griol-Charhbili2005 ¹⁰⁹	N	Y	N	?	L	?	?	?	?	?	?	L
Gross1992 ¹¹⁰	Y	N	N	?	?	?	?	?	?	?	L	L
Gross2009 ¹¹¹	N	N	N	H	?	?	?	?	?	?	L	L
Grover1992 ¹¹²	N	N	N	?	?	?	?	?	?	?	?	L
Grover1996 ¹¹³	N	N	N	?	?	?	?	?	?	?	L	L
Grund1997 ¹¹⁴	Y	N	N	?	?	?	?	?	?	?	L	L
Gu2008 ¹¹⁵	Y	N	N	?	?	?	?	?	?	?	L	L
Gumina1999 ¹¹⁶	Y	N	N	?	?	?	?	?	?	?	L	L
Gumina2001 ¹¹⁷	Y	N	N	?	?	?	?	?	?	?	L	L
Gumina2005 ¹¹⁸	N	N	N	?	?	?	?	?	?	?	L	L
Guo1998 ¹¹⁹	N	N	N	?	L	?	?	?	?	?	?	L
Guo1999 ¹²⁰	N	N	N	?	?	?	?	?	?	?	?	L
Guo2001 ¹²¹	N	N	N	?	L	?	?	?	?	?	?	L
Guo2007 ¹²²	N	N	N	?	?	?	?	?	?	?	?	L
Guo2012 ¹²³	N	N	N	?	L	?	?	?	?	?	L	L
Gysembergh1998 ¹²⁴	N	N	N	?	?	?	?	?	?	?	?	L
Haessler1994 ¹²⁵	Y	N	N	?	?	?	?	?	?	?	L	L
Haessler1997 ¹²⁶	Y	N	N	?	?	?	?	?	?	?	L	L
Hale1992 ¹²⁷	Y	N	N	?	L	?	?	?	?	?	H	L
Hale1999 ¹²⁸	Y	N	N	?	L	?	?	?	?	?	H	H
Halkos2004 ¹²⁹	Y	N	N	?	?	?	?	?	?	?	?	L
Hampton2003 ¹³⁰	N	Y	N	?	?	?	?	?	?	?	L	L
Haruna1998 ¹³¹	Y	N	N	?	L	?	?	?	?	?	?	L
Hatori2001 ¹³²	Y	Y	N	L	?	?	?	?	?	?	L	L
Hausenloy2012 ¹³³	Y	N	N	?	?	?	?	?	?	?	?	L
He2009 ¹³⁴	Y	N	N	?	?	?	?	?	?	?	L	L
Heinen2011 ¹³⁵	Y	N	N	?	L	?	?	?	?	?	?	L

Supplemental Table B - study quality and risk of bias - page 6 of 12

study	reporting - randomization	reporting - blinding	reporting - power calculation	bias - random group allocation	bias - groups similar at baseline	bias - blinded group allocation	bias - random housing	bias - blind intervention	bias - random outcome assessment	bias - blind outcome assessment	bias - reporting of drop-outs	bias - other
Li_X2012b ²²⁶	Y	Y	N	?	?	?	?	?	?	?	L	L
Li_Y1992a ²²⁷	Y	N	N	?	?	?	?	?	?	?	?	H
Li_Y1992b ²²⁸	Y	Y	N	?	?	?	?	H	?	?	?	H
Li_Y1993a ²²⁹	Y	Y	N	?	L	?	?	L	?	?	?	L
Li_Y1993b ²³⁰	Y	Y	N	?	L	?	?	L	?	?	?	L
Li_Y1994 ²³¹	Y	N	N	?	L	?	?	?	?	?	?	L
Li_Y1995 ²³²	Y	N	N	?	L	?	?	?	?	?	?	L
Li_Y2011 ²³³	N	N	N	?	?	?	?	?	?	?	?	L
Liao2013 ²³⁴	Y	N	N	L	?	?	?	?	?	?	H	L
Liudet2001 ²³⁵	N	N	N	?	?	?	?	?	?	?	?	L
Lie2010 ²³⁶	Y	N	N	?	L	?	?	?	?	L	?	L
Liem2001 ²³⁷	N	N	N	?	L	?	?	?	?	?	L	L
Liem2005 ²³⁸	N	N	N	?	L	?	?	?	?	?	?	L
Lim2007 ²³⁹	N	N	N	?	?	?	?	?	?	?	?	L
Lim2010 ²⁴⁰	Y	N	N	?	L	?	?	?	?	?	?	L
Liu1993a ²⁴¹	Y	N	N	?	L	?	?	?	?	?	?	L
Liu1993b ²⁴²	Y	N	N	?	L	?	?	?	?	?	L	L
Liu1994 ²⁴³	N	N	N	?	?	?	?	?	?	?	L	L
Liu2005 ²⁴⁴	Y	N	N	?	?	?	?	?	?	?	?	L
Liu2008 ²⁴⁵	N	N	N	?	?	?	?	?	?	?	L	L
LiuG1992a ²⁴⁶	Y	N	N	?	?	?	?	?	?	?	?	H
LiuG1992b ²⁴⁷	Y	N	N	?	?	?	?	?	?	?	?	L
LiuY1992 ²⁴⁸	Y	N	N	?	?	?	?	?	?	?	?	L
Loke1998 ²⁴⁹	Y	N	N	?	?	?	?	?	?	?	?	L
Lott1996 ²⁵⁰	Y	N	N	?	L	?	?	?	?	?	?	L
Lotz2011 ²⁵¹	Y	N	N	?	L	?	?	?	?	?	?	H
Lou2003 ²⁵²	Y	N	N	?	?	?	?	?	?	?	?	L
Lu2009 ²⁵³	N	N	N	?	?	?	?	?	?	?	?	L
Lu2011 ²⁵⁴	Y	N	N	?	L	?	?	?	?	?	?	L
Lu2012 ²⁵⁵	Y	N	N	?	L	?	?	?	?	?	L	L
Luo2004 ²⁵⁶	Y	N	N	?	?	?	?	?	?	?	?	L
Manintveld2005 ²⁵⁷	N	N	N	?	L	?	?	?	?	?	?	L
Manintveld2011 ²⁵⁸	N	N	N	?	?	?	?	?	?	?	?	L
Marber1993 ²⁵⁹	N	N	N	H	?	?	?	?	?	?	H	H
Martin1997 ²⁶⁰	N	N	N	?	?	?	?	?	?	?	?	L
Matsuda1993 ²⁶¹	N	N	N	?	?	?	?	?	?	?	H	L
Matsumura2000 ²⁶²	N	N	N	?	L	?	?	?	?	?	L	L
McVey1999a ²⁶³	N	N	N	?	L	?	?	?	?	?	L	L
McVey1999b ²⁶⁴	N	N	N	?	?	?	?	?	?	?	?	L
Mei1998 ²⁶⁵	Y	N	N	?	?	?	?	?	?	?	L	L
Miki1996 ²⁶⁶	Y	N	N	?	L	?	?	?	?	?	L	L
Miki1998a ²⁶⁷	N	N	N	?	?	?	?	?	?	?	L	L
Miki1998b ²⁶⁸	N	N	N	?	L	?	?	?	?	?	L	L
Miki1999 ²⁶⁹	N	N	N	?	?	?	?	?	?	?	L	H
Miller1999 ²⁷⁰	Y	Y	N	?	?	?	?	?	?	L	?	L

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study	reporting - randomization	reporting - blinding	reporting - power calculation	bias - random group allocation	bias - groups similar at baseline	bias - blinded group allocation	bias - random housing	bias - blind intervention	bias - random outcome assessment	bias - blind outcome assessment	bias - reporting of drop-outs	bias - other
Minamino1996 ²⁷¹	N	N	N	?	?	?	?	?	?	?	?	L
Miura1991 ²⁷²	Y	N	N	?	L	?	?	?	?	?	L	L
Miura1992 ²⁷³	N	N	N	?	L	?	?	?	?	?	L	L
Miura1998 ²⁷⁴	Y	N	N	H	L	?	?	?	?	?	L	L
Mizumura1995 ²⁷⁵	Y	N	N	?	?	?	?	?	?	?	L	L
Mizumura1996 ²⁷⁶	N	N	N	?	?	?	?	?	?	?	L	L
Mizumura1997 ²⁷⁷	Y	N	N	?	?	?	?	?	?	?	?	L
Morgan1999 ²⁷⁸	Y	N	N	?	?	?	?	?	?	?	?	L
Mortensen2006 ²⁷⁹	N	N	N	?	?	?	?	?	?	?	?	L
Mullenheim2001a ²⁸⁰	N	N	N	?	L	?	?	?	?	?	?	L
Mullenheim2001b ²⁸¹	Y	N	N	?	L	?	?	?	?	?	?	L
Mullenheim2001c ²⁸²	Y	N	N	?	L	?	?	?	?	?	?	L
Mullenheim2003 ²⁸³	N	N	N	?	?	?	?	?	?	?	?	L
Munch-Ellingsen1997 ²⁸⁴	N	N	N	?	?	?	?	?	?	?	L	L
Munch-Ellingsen1998 ²⁸⁵	N	N	N	?	?	?	?	?	?	?	L	L
Murry1986 ²⁸⁶	Y	N	N	?	?	?	?	?	?	?	L	L
Murry1991 ²⁸⁷	N	N	N	?	?	?	?	?	?	?	H	H
Nadtochiy2009 ²⁸⁸	N	N	N	?	L	?	?	?	?	?	?	L
Nakae2000 ²⁸⁹	N	N	N	?	L	?	?	?	?	?	L	L
Nakano1997 ²⁹⁰	N	N	N	?	L	?	?	?	?	?	?	L
Naumenko2010 ²⁹¹	Y	N	N	?	?	?	?	?	?	?	?	L
Nawada1997 ²⁹²	N	N	N	?	L	?	?	?	?	?	L	L
Neckar2002 ²⁹³	N	N	N	?	L	?	?	?	?	?	L	L
Nieszner2002 ²⁹⁴	N	N	N	?	?	?	?	?	?	?	?	L
Nishihara2006 ²⁹⁵	N	N	N	?	L	?	?	?	?	?	?	L
Nithipatikom2006a ²⁹⁶	N	N	N	H	?	?	?	?	?	?	?	L
Nithipatikom2006b ²⁹⁷	N	N	N	H	?	?	?	?	?	?	?	L
Node1997 ²⁹⁸	Y	N	N	?	?	?	?	?	?	?	L	L
Nozawa1999 ²⁹⁹	Y	Y	N	?	?	L	?	L	?	L	L	L
Nozawa2003 ³⁰⁰	N	N	N	?	L	?	?	?	?	?	?	L
Okamura1999 ³⁰¹	Y	N	N	?	L	?	?	?	?	?	?	L
Okubo2000 ³⁰²	Y	N	N	?	L	?	?	?	?	?	L	L
Okubo2004a ³⁰³	Y	N	N	?	L	?	?	?	?	?	H	L
Okubo2004b ³⁰⁴	N	N	N	?	L	?	?	?	?	?	?	L
Ovize1992 ³⁰⁵	Y	N	N	?	?	?	?	?	?	?	L	L
Ovize1995 ³⁰⁶	Y	N	N	?	?	?	?	?	?	?	L	L
Pagel2007 ³⁰⁷	Y	N	N	?	L	?	?	?	?	?	L	L
Patel2001 ³⁰⁸	Y	N	N	?	L	?	?	?	?	?	?	L
Patel2002 ³⁰⁹	Y	N	N	?	L	?	?	?	?	?	?	L
Patel2005 ³¹⁰	N	N	N	?	L	?	?	?	?	?	L	L
Peart2003 ³¹¹	Y	N	N	?	?	?	?	?	?	?	?	L
Pell1998 ³¹²	Y	Y	N	?	L	?	?	?	L	?	?	L
Perricone2013 ³¹³	N	Y	N	?	?	?	?	?	L	?	?	L
Petrishchev2006 ³¹⁴	N	N	N	?	?	?	?	?	?	?	?	L
Ping1999 ³¹⁵	N	N	N	?	L	?	?	?	?	?	L	L

Supplemental Table B - study quality and risk of bias - page 8 of 12

study	reporting - randomization	reporting - blinding	reporting - power calculation	bias - random group allocation	bias - groups similar at baseline	bias - blinded group allocation	bias - random housing	bias - blind intervention	bias - random outcome assessment	bias - blind outcome assessment	bias - reporting of drop-outs	bias - other
Ping2002 ³¹⁶	N	N	N	?	?	?	?	?	?	?	?	L
Piot1997 ³¹⁷	Y	N	N	?	?	?	?	?	?	?	?	L
Poulsen2014 ³¹⁸	N	N	N	?	?	?	?	?	?	?	L	L
Przyklenk1993 ³¹⁹	Y	Y	N	?	?	?	?	?	?	L	?	L
Przyklenk1995 ³²⁰	Y	N	N	?	?	?	?	?	?	?	L	L
Przyklenk1996 ³²¹	Y	Y	N	?	?	?	?	?	?	L	H	H
Przyklenk1997 ³²²	Y	N	N	?	?	?	?	?	?	?	L	L
Przyklenk2001 ³²³	Y	N	N	?	?	?	?	?	?	?	?	L
Przyklenk2003 ³²⁴	Y	Y	N	?	?	?	?	?	?	L	?	L
Qian1996 ³²⁵	Y	N	N	?	?	?	?	?	?	?	?	L
Qian1999 ³²⁶	N	N	N	?	L	?	?	?	?	?	?	L
Qiu1997a ³²⁷	N	N	N	?	L	?	?	?	?	?	L	L
Qiu1997b ³²⁸	N	N	Y	?	?	?	?	?	?	?	L	L
Rajesh2003 ³²⁹	Y	N	N	?	L	?	?	?	?	?	?	L
Rajesh2004 ³³⁰	N	N	N	?	L	?	?	?	?	?	?	L
Raphael2005 ³³¹	Y	N	N	?	?	?	?	?	?	?	L	L
Redel2009 ³³²	Y	Y	N	?	L	?	?	?	?	L	L	L
Reffellmann2003 ³³³	Y	N	N	?	L	?	?	?	?	?	?	H
Ren2004 ³³⁴	N	N	N	?	?	?	?	?	?	?	L	L
Richard1993 ³³⁵	N	N	N	?	L	?	?	?	?	?	?	H
Richard1994 ³³⁶	N	N	N	?	?	?	?	?	?	?	?	L
Rioufol1997 ³³⁷	Y	N	N	L	?	?	?	?	?	?	L	L
Rivo2006 ³³⁸	Y	N	N	?	?	?	?	?	?	?	L	L
Roesner2007 ³³⁹	Y	N	N	?	L	?	?	?	?	L	L	L
Roesner2010 ³⁴⁰	N	Y	N	?	L	?	?	?	?	L	L	L
Rohmann1994 ³⁴¹	N	N	N	?	?	?	?	?	?	?	L	L
Sack1993 ³⁴²	N	N	N	?	L	?	?	?	?	?	?	L
Sanada2001a ³⁴³	N	N	N	?	?	?	?	?	?	?	L	L
Sanada2001b ³⁴⁴	Y	Y	N	?	?	?	?	?	?	L	?	L
Sanada2004 ³⁴⁵	N	N	N	?	?	?	?	?	?	?	L	L
Sandhu1997 ³⁴⁶	N	N	N	?	?	?	?	?	?	?	?	L
Sanz1995 ³⁴⁷	Y	Y	N	?	?	?	?	?	L	L	L	L
Sarkar2012 ³⁴⁸	N	N	N	?	?	?	?	?	?	?	?	L
Sasamori2006 ³⁴⁹	Y	N	N	?	?	?	?	?	?	?	?	L
Sato2007 ³⁵⁰	N	N	N	?	L	?	?	?	?	?	L	L
Sbarouni2006 ³⁵¹	N	N	N	?	L	?	?	?	?	?	H	L
Schmidt2014 ³⁵²	Y	Y	N	?	?	?	?	?	?	L	L	L
Schoemaker2000 ³⁵³	N	N	N	?	L	?	?	?	?	?	?	L
Schott1990 ³⁵⁴	Y	N	N	?	L	?	?	?	?	?	L	L
Schultz1995 ³⁵⁵	Y	N	N	?	L	?	?	?	?	?	L	L
Schultz1996 ³⁵⁶	Y	N	N	?	L	?	?	?	?	?	L	L
Schultz1997a ³⁵⁷	Y	N	N	?	?	?	?	?	?	?	?	L
Schultz1997b ³⁵⁸	Y	N	N	?	L	?	?	?	?	?	L	L
Schultz1997c ³⁵⁹	Y	N	N	?	L	?	?	?	?	?	?	H
Schultz1997d ³⁶⁰	Y	N	N	?	L	?	?	?	?	?	?	H

Supplemental Table B - study quality and risk of bias - page 10 of 12

study	reporting - randomization	reporting - blinding	reporting - power calculation	bias - random group allocation	bias - groups similar at baseline	bias - blinded group allocation	bias - random housing	bias - blind intervention	bias - random outcome assessment	bias - blind outcome assessment	bias - reporting of drop-outs	bias - other
Thornton1992 ⁴⁰⁶	N	N	N	H	?	H	?	?	?	?	L	L
Thornton1993a ⁴⁰⁷	N	N	N	H	?	?	?	?	?	?	?	L
Thornton1993b ⁴⁰⁸	Y	N	N	?	?	?	?	?	?	?	?	L
Thornton1993c ⁴⁰⁹	N	N	N	?	?	?	?	?	?	?	L	L
Tissier2001 ⁴¹⁰	Y	N	N	?	L	?	?	?	?	?	L	L
Tissier2002 ⁴¹¹	Y	N	N	?	L	?	?	?	?	?	?	L
Toller1999 ⁴¹²	Y	N	N	?	?	?	?	?	?	?	L	L
Toombs1993a ⁴¹³	N	Y	N	?	?	?	?	?	?	L	?	L
Toufektsian2003 ⁴¹⁴	Y	N	N	?	L	?	?	?	?	?	?	L
Toyoda2000 ⁴¹⁵	Y	N	N	?	?	?	?	?	?	?	L	L
Tranter2010 ⁴¹⁶	N	N	Y	?	?	?	?	?	?	?	?	L
Tsovolas2008 ⁴¹⁷	Y	N	N	?	?	?	?	?	?	?	?	L
Tsuchida1992 ⁴¹⁸	N	N	N	?	L	?	?	?	?	?	L	L
Tsuchida1994a ⁴¹⁹	Y	N	N	?	?	?	?	?	?	?	L	L
Tsuchida1994b ⁴²⁰	Y	N	N	?	?	?	?	?	?	?	L	L
Tsuchida1998 ⁴²¹	Y	N	N	?	L	?	?	?	?	?	L	L
Turan2008 ⁴²²	N	N	N	?	?	?	?	?	?	?	?	L
Ueda1999 ⁴²³	Y	N	N	?	?	?	?	?	?	?	?	L
Uematsu1998 ⁴²⁴	Y	N	N	?	?	?	?	?	?	?	L	L
Valtchanova2004 ⁴²⁵	N	N	N	?	?	?	?	?	?	?	?	L
Valtchanova-Matchouganska2003 ⁴²⁶	Y	N	N	?	?	?	?	?	?	?	?	L
VandenDoel1998 ⁴²⁷	N	N	N	?	L	?	?	?	?	?	L	L
VanderHeide1994 ⁴²⁸	N	N	N	?	?	?	?	?	?	?	L	L
VanWinkle1994b ⁴²⁹	N	N	N	?	?	?	?	?	?	?	L	L
VanWynlen1994 ⁴³⁰	N	N	N	?	?	?	?	?	?	?	L	L
Vetterlein2006 ⁴³¹	N	N	N	?	L	?	?	?	?	?	?	L
Vincent2012 ⁴³²	Y	N	N	?	?	?	?	?	?	?	?	L
Virag2013 ⁴³³	N	N	N	?	?	?	?	?	?	?	?	L
Vladic2011 ⁴³⁴	Y	N	N	?	L	?	?	?	?	?	?	L
Vogt1998 ⁴³⁵	N	N	N	?	L	?	?	?	?	?	L	L
Vogt2001 ⁴³⁶	N	Y	N	?	?	?	?	?	?	?	?	L
Wall1994 ⁴³⁷	Y	N	N	?	?	?	?	?	?	?	?	H
Walsh1994 ⁴³⁸	N	N	N	?	?	?	?	?	H	?	?	L
Wang2001 ⁴³⁹	Y	N	N	?	L	?	?	?	?	?	L	L
Wang2002 ⁴⁴⁰	Y	N	N	?	L	?	?	?	?	?	L	L
Wang2009 ⁴⁴¹	Y	N	N	?	?	?	?	?	?	?	?	L
WangS2004 ⁴⁴²	Y	N	N	?	L	?	?	?	?	?	L	L
WangY2004 ⁴⁴³	N	N	N	?	L	?	?	?	?	?	?	H
Watanabe2006 ⁴⁴⁴	N	N	N	?	L	?	?	?	?	?	L	L
Weber2005 ⁴⁴⁵	N	N	N	?	?	?	?	?	?	?	?	H
Weber2008 ⁴⁴⁶	Y	N	Y	L	?	?	?	?	?	?	?	L
Weinbrenner2002 ⁴⁴⁷	N	N	N	?	?	?	?	?	?	?	?	L
Weinbrenner2004 ⁴⁴⁸	N	N	N	?	H	?	?	?	?	?	?	L
Wolfe1993 ⁴⁴⁹	N	N	N	?	?	?	?	?	?	?	L	L
Wolfrum2002 ⁴⁵⁰	Y	N	N	?	L	?	?	?	?	?	?	L

Supplemental Table B - study quality and risk of bias - page 12 of 12

study	reporting - randomization	reporting - blinding	reporting - power calculation	bias - random group allocation	bias - groups similar at baseline	bias - blinded group allocation	bias - random housing	bias - blind intervention	bias - random outcome assessment	bias - blind outcome assessment	bias - reporting of drop-outs	bias - other
ZhangS2006 ⁴⁹⁶	N	N	N	?	?	?	?	?	?	?	?	L
ZhangX2006 ⁴⁹⁷	Y	N	N	?	?	?	?	?	?	?	L	L
Zhao2003 ⁴⁹⁸	Y	N	N	?	?	?	?	?	?	?	?	H
Zhao2012 ⁴⁹⁹	N	N	N	?	?	?	?	?	?	?	?	L
Zhu2007 ⁵⁰⁰	N	Y	N	?	?	?	?	?	?	L	?	L
Zhu2009 ⁵⁰¹	Y	N	N	?	L	?	?	?	?	?	?	L
Zhu2011 ⁵⁰²	Y	N	N	?	L	?	?	?	?	?	?	H
Zhu2013 ⁵⁰³	Y	Y	N	?	L	?	?	?	?	L	?	L

Meta-analysis includes data from 785 independent comparisons identified from 503 studies. Y = yes, N = not reported, ? = unclear risk of bias, L = low risk of bias, H = high risk of bias.

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Supplemental table C - Meta-analysis study quality

	# pub	# comp (%)	MD [95%CI]
all (T^2 164.4, I^2 94.7%)	503	785 (100)	24.6 [23.5, 25.6]
reported randomization			
P>0.11, adj. R^2 = 0.42%			
not reported	258	420 (54)	25.3 [24.0, 26.7]
yes	245	365 (47)	23.7 [21.7, 25.7]
<i>rodents</i>			
P>0.98, adj. R^2 = -0.33%			
not reported	198	200 (58)	26.8 [24.9, 28.7]
yes	185	144 (42)	26.8 [24.9, 28.7]
<i>non-rodents</i>			
P>0.10, adj. R^2 = 0.80%			
not reported	60	220 (50)	23.9 [22.0, 25.8]
yes	60	221 (50)	21.7 [19.8, 23.6]
reported blinding			
P>0.69, adj. R^2 = -0.15%			
not reported	447	707 (90)	24.5 [23.5, 25.5]
yes	56	78 (10)	25.2 [21.9, 28.5]
<i>rodents</i>			
P>0.43, adj. R^2 = -0.03%			
not reported	345	315 (92)	27.0 [25.4, 28.5]
yes	38	29 (8)	24.9 [23.3, 26.4]
<i>non-rodents</i>			
P>0.17, adj. R^2 = 0.21%			
not reported	102	392 (89)	22.4 [21.0, 23.8]
yes	18	49 (11)	25.3 [23.9, 26.7]
random group allocation (selection bias)			
P>0.92, adj. R^2 = -0.28%			
high	11	14 (2)	23.2 [16.0, 30.3]
low	10	11 (1)	25.0 [13.9, 36.0]
unclear	482	760 (97)	24.6 [17.4, 31.8]
groups similar at baseline (selection bias)			
P>0.01, adj. R^2 = 1.24%			
high	5	8 (1)	27.1 [17.4, 36.8]
low	207	344 (44)	26.2 [16.4, 36.0]
unclear	291	433 (55)	23.2 [13.5, 33.0]
blinded group allocation (selection bias)			
not analyzed			
high	2	2 (0.3)	30.5 [11.6, 49.4]
low	1	1 (0.1)	16.2 [-18.1, 50.5]
unclear	500	782 (99)	24.6 [5.6, 43.5]

Supplemental table C (continued) - Meta-analysis study quality

	# pub	# comp (%)	MD [95%CI]
random housing (performance bias)			
not analyzed			
high	1	1 (0.1)	31.0 [4.8, 57.2]
low	0	0 (0)	NA [NA]
unclear	502	784 (99)	24.6 [-1.6, 50.8]
blind intervention (performance bias)			
not analyzed			
high	2	2 (0.3)	30.4 [10.6, 50.3]
low	3	3 (0.4)	27.1 [0.8, 53.3]
unclear	498	780 (99)	24.5 [4.7, 44.4]
random outcome assessment (detection bias)			
not analyzed			
high	1	1 (0.1)	31.0 [4.8, 57.2]
low	1	1 (0.1)	17.1 [-21.3, 55.5]
unclear	501	783 (99)	24.6 [-1.7, 50.8]
blind outcome assessment (detection bias)			
P>0.87, adj. R ² = -0.28%			
high	2	2 (0.3)	29.5 [10.9, 48.1]
low	40	52 (7)	24.6 [5.6, 43.6]
unclear	461	731 (93)	24.5 [6.0, 43.1]
reporting of drop-outs (attrition bias)			
P>0.01, adj. R ² = 1.29%			
high	27	42 (5)	24.4 [20.3, 28.5]
low	226	340 (43)	22.9 [18.5, 27.3]
unclear	250	403 (51)	26.0 [21.7, 30.4]

Total # comparisons = 8, corrected P<0.006; pub = publications, comp = comparisons, NA = not applicable, adj. = adjusted, MD = weighted difference in means, RoB = risk of bias, ass. = assessment.

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