

**Suppl. Table S1.** Level of evidence and risk of bias assessment; indication of the reliability of the included studies.

Study	n	Control group	Random allocation	Level of evidence <sup>a</sup>	Study design	Blinding	Selective reporting bias	Missing data verified bias	Follow up bias	Confounding factor	Comparable groups bias
Kouloulis et al. 2002 [57]	37	Yes	No	3	Pro	No	Low	–	NR	Low	Low
Ohguri et al. 2008 [60]	29	Yes	No	3	Retro	No	Low	Low	Low	High	Low
Yamada et al. 1992 [54]	73	Yes	No	3	Retro	No	High	–	NR	High	Low
Maluta et al. 2011 [62]	68	Yes	No	3	Pro	No	Low	High	Low	High	Medium
Ashayeri et al. 1993 [55]	24	Yes	No	4	Retro	No	Low	Low	NR	Low	Low
Maebayashi et al. 2017 [66]	13	Yes	No	3	Retro	No	Low	–	NR	High	Medium
Douwes 2006 [58]	30	No	–	4	Retro	No	Low	–	NR	Low	–
Tschoep-Lechner et al. 2013 [64]	23	No	–	4	Retro	No	Low	Low	NR	High	–
Volovat et al. 2014 [65]	19	No	–	4	Pro	No	Low	Low	NR	High	–
Ishikawa et al. 2012 [63]	18	No	–	4	Phase II	No	Low	–	NR	Low	–
Bakshandeh-Bath et al. 2009 [61]	13	No	–	4	Retro	No	Low	–	NR	Low	–
Kouloulis et al. 2001 [56]	7	No	–	4	Pro	No	Low	–	Low	Low	–
Kakehi et al. 1990 [53]	34	No	–	4	Retro	No	Low	–	NR	High	–
Bull et al. 2008 [59]	7	No	–	4	Phase I/II	No	Low	–	NR	High	–
<b>Overall</b>	<b>395</b>	<b>6/14</b>	<b>0/6</b>	<b>3–4</b>							
		<b>(43%)</b>									

–, not applicable; NR, not reported; Retro, retrospective; Pro, prospective

<sup>a</sup> OCEBM level 3: Non-randomized controlled cohort/follow-up study; level 4: Case-series, case-control studies, or historically controlled studies [40]