

Hitoshi Yokoyama

Abstract

Coronary artery bypass surgery is a microsurgery. Stabilization of the coronary artery on the beating heart is the key concept for successful off-pump coronary artery bypass surgery. Recent progress in 3-dimensional motion capture and reconstruction technology is revealing the quantitative characteristics of coronary artery motion in detail. Various factors such as cardiac contractility, heart rate, mechanical ventilation, and coronary artery anatomy have great influence on the coronary artery motion. The effect of various stabilization or anti-stabilization technique such as suction-type mechanical tissue stabilizer, beta-adrenoreceptor blockers, vasopressors, heart pacing, and ventilation is analyzed and discussed for better understanding of optimizing the stabilization of coronary artery anastomosis site.

Keywords

Suction-type tissue stabilizer • Evaluation for stabilization • Pharmacological stabilization • Landiolol hydrochloride

10.1 Stabilization Is the Key for Successful Off-Pump Coronary Artery Bypass Surgery

10.1.1 Hypothesis: Stabilization-Patency Relationship

Off-pump coronary artery bypass is a microsurgery, in which a surgeon works on small moving object. Error of microstitches on the small vessels may result in graft stenosis and occlusion. Studies of human performance show the range in technical error of surgeon with high-power magnification glasses is between 0.1 and 0.2 mm if he or she has a good hand [1]. Assuming a surgeon is working on a coronary artery of 1–2 mm in diameter, the error of suture could be up to 20 % in maximum.

There are miscellaneous factors affecting coronary artery motion (Fig. 10.1). Every effort should be paid to avoid or control these factors for better stabilization.

Here is a hypothesis or assumption on the relationship among stabilization, surgeon skill, and graft patency. Intuitively, residual motion of the anastomosis sites under efforts for stabilization affects the graft patency (Fig. 10.2). When the residual motion is acceptable for the surgeon, he or she feels comfortable enough to place precise stitches, making a good anastomosis with excellent graft patency. If the residual motion of anastomosis site were too big to make an acceptable anastomosis, expected graft patency would decrease dramatically.

Surgeon's skill is another factor for graft patency. The stabilization-patency relationship can be shifted to left by surgical training. The expert surgeon is able to manage to work on the moving coronary artery somehow, while the surgical resident is not. However, there is a human limit for working on a moving small target even for the expert surgeon. Thus, here is a hypothesis that these 2 factors, stabilization and surgeon skill, may affect the configuration of the

H. Yokoyama (✉)
Department of Cardiovascular Surgery, Fukushima Medical
University, 1 Hikarigaoka, Fukushima 960-1295, Japan
e-mail: hitoshiy@fmu.ac.jp

Factors for stabilization

- Heart
 - Chronotropic state: heart rate
 - Inotropic state: contractility
 - preload / afterload
 - sympathetic / parasympathetic nerve tone
 - serum catecholamine (intrinsic / extrinsic)
 - Coronary artery anatomy
 - Surrounding fat
- Adjacent organ movement
 - Lung ventilation
- Mechanical stabilization
 - Suction-type tissue stabilizer
 - Additional tips
- Pharmacological stabilization
 - Inotropic agents
 - Vasopressors

Fig. 10.1 Factors influencing the stabilization of the coronary artery on a beating heart

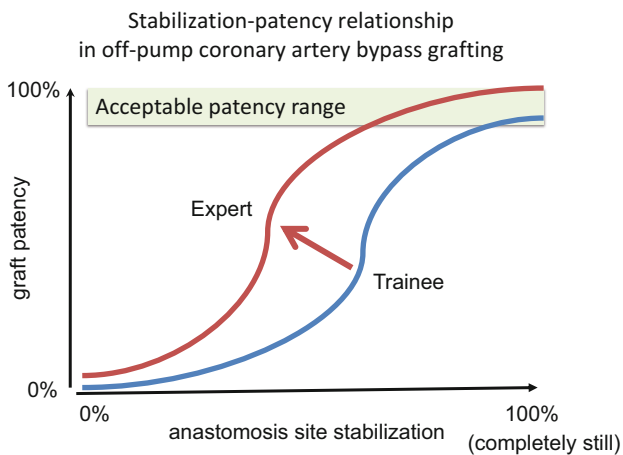


Fig. 10.2 Hypothesis: stabilization-patency relationship in off-pump coronary artery bypass grafting. For trainees with less experience, acceptable graft patency can be achieved only when the anastomosis site stabilization is near perfect (100%). For expert surgeons, acceptable graft patency can be achieved as long as the anastomosis site stabilization is not poor. This relationship curve can be shifted to the left by surgical skill training

anastomosis and graft patency. Therefore, surgical training (see Chap. 26: Teaching and training) and stabilization is the key for successful off-pump coronary artery surgery. Here comes the next question: regarding the stabilization, how good is good enough for surgeons to provide an acceptable graft patency?

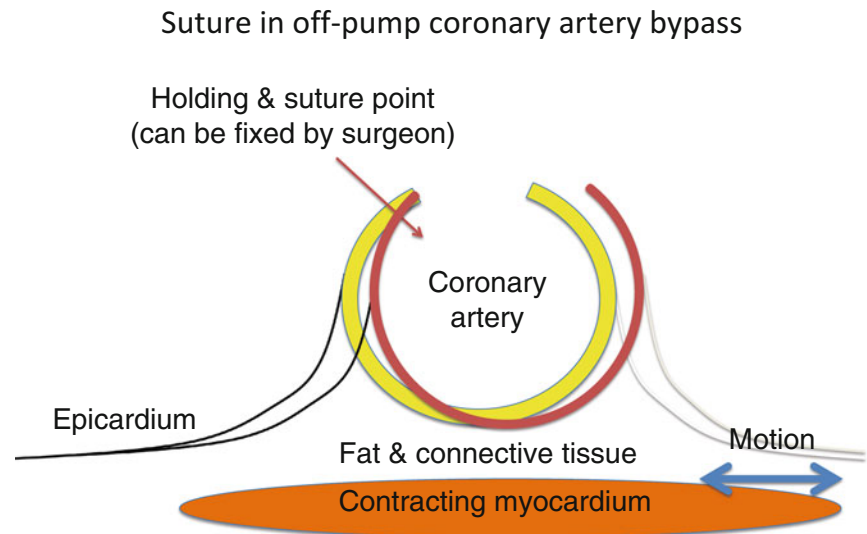
10.1.2 How Good Is Good Enough for Stabilization?

An expert off-pump surgeon can make a good stitch on the moving coronary artery. However, there is a human limit of acceptable motion of the target. Figure 10.3 shows a scheme of suturing the moving coronary artery. The task of a surgeon is to hold the coronary artery adventitia and make a precise stitch without laceration of the wall. The coronary artery wall is soft and flexible and can be held to make immobile point even on the moving floor made with myocardium and fat tissue. Try to hold the coronary artery wall by forceps. If it can be held to be immobile without any tension, a surgeon can make an incision and stitches. If a surgeon feels any traction force on the holding point, delicate procedure around the holding point on the coronary wall without a risk of laceration is not recommended. In summary, a surgeon can confirm if he or she obtains an acceptable stabilization by holding the target coronary artery wall in static position.

10.2 Evaluation of Stabilization

The motion of target anastomosis areas during off-pump coronary artery bypass is an important issue for cardiac surgeons. Several attempts for evaluating the cardiac surface motion in a quantitative fashion have been reported. In 1996, Borst and associates [2] reported that a mechanical stabilizer (Octopus) significantly reduced the area circumscribed by the 2-dimensional reference points on the right coronary artery and obtuse marginal branch in pigs by using an analog video camera. In 2002, Dettler and associates [3] measured the deviation of small vessels in the anterior wall by using an orthogonal polarizations spectral imaging device, reporting that the deviation was significantly decreased with mechanical stabilizers. They also showed better stabilization is associated with shorter anastomosis time. In 2003, Koransky and associates [4] 3-dimensionally reconstructed the motion of the left anterior descending artery with digital sonomicrometry. They reported that mechanical stabilization significantly reduced the 3-dimensional excursion, maximum velocity, and average velocity. In 2004, Cattin and associates [5] captured the wall movements of the beating heart by using a high-speed camera coupled with a laser sensor, analyzing the trajectory of the point of interest. In their system, the 2-dimensional lateral motion (x -, y -axis) was captured with the high-speed camera, and the out-of-plane motion (z -axis) was acquired with the laser sensor. In 2005, Lemma and associates [6] captured the coronary artery simultaneously with two digital cameras, reconstructing the wall movements of the heart in 3-dimensional fashion. They quantitatively reported the distance of marker displacement

Fig. 10.3 Suture in off-pump coronary artery bypass grafting. The bases of the coronary arteries are fixed to the contracting myocardium. The coronary artery wall can be held immobile, because the wall and surrounding fat are flexible



on the beating heart in the Cartesian coordinate system (x -, y -, z -axis) before and after stabilization.

Most recently, Watanabe and associates developed a 3-dimensional digital motion capture and reconstruction system [7], which is an application of modern robotic technology (Fig. 10.4). The new digital system is able to reconstruct the 3-dimensional motion of any coronary arteries such as distance moved, velocity, acceleration, and deceleration in every region and every axis. By the use of an endoscope with high-speed camera (955 frames per second), accuracy of mean resolution ($70 \pm 6 \mu\text{m}$) and time resolution of 3-dimensional data points (480 xyz position data per second) are improved. The endoscope and the small lightweight markers for tracking can be sterilized and used in any clinical procedure. In the following chapters, several studies using this system are introduced.

10.3 Tissue Stabilizers

10.3.1 Pre-Octopus Era: Tape, Snare, etc

In the previous era before Octopus or other suction-type tissue stabilizer, many efforts to stabilize the coronary anastomosis site were reported [8–12]. These efforts include tape, snare, and stitches around the target coronary artery, which are still useful in addition of the current suction-type tissue stabilizer. Because the effects of tissue stabilization depends on the local factor such as fat deposition around the anastomosis site and the tortuosity of the target coronary artery, few stitches around the coronary anastomosis site with traction, for example, may provide further stabilization. The off-pump surgeon needs to know the history and should apply these inexpensive, simple, and effective techniques when appropriate.

10.3.2 Suction-Type Tissue Stabilizer

In 1996, Borst and colleagues developed Octopus tissue stabilizer, which immobilizes the epicardium using a suction device [2]. Jansen and colleagues used this device for the patients who underwent off-pump coronary artery bypass [13]. With an aid of the Octopus tissue stabilizer, off-pump technique became popular in the late 1990s. Several suction-type tissue stabilizers are now available (Fig. 10.5), becoming the common, simple modality for off-pump coronary artery bypass surgery.

In an animal study, Watanabe and associates [7] found that mechanical stabilization (Octopus) can reduce the distance moved during one cardiac cycle remarkably, while the rapid, sudden movements such as maximal velocity, acceleration, and deceleration are not decreased much (Fig. 10.6). In detail, the distance moved in one cardiac cycle is decreased to 15.9 % of the baseline value (84.1 % reduction below the baseline when the baseline value is assumed as 100 %) in the left anterior descending artery by the Octopus stabilization, while maximum velocity, acceleration, and deceleration is only decreased to 62.5 % (37.5 % reduction), 65.3 % (34.7 % reduction), and 64.1 % (35.9 % reduction), respectively. In other words, “sudden quick motion” remains even under the most recent sophisticated mechanical tissue stabilizer. Several efforts to decrease these sudden quick motions are introduced in the following sections.

10.4 Pharmacological Stabilization: Beta-Blocker

β -adrenergic receptors are mainly located in the heart, blood vessels, and bronchi. β_1 -receptor blockers decrease heart rate (negative chronotropic effect) and myocardial

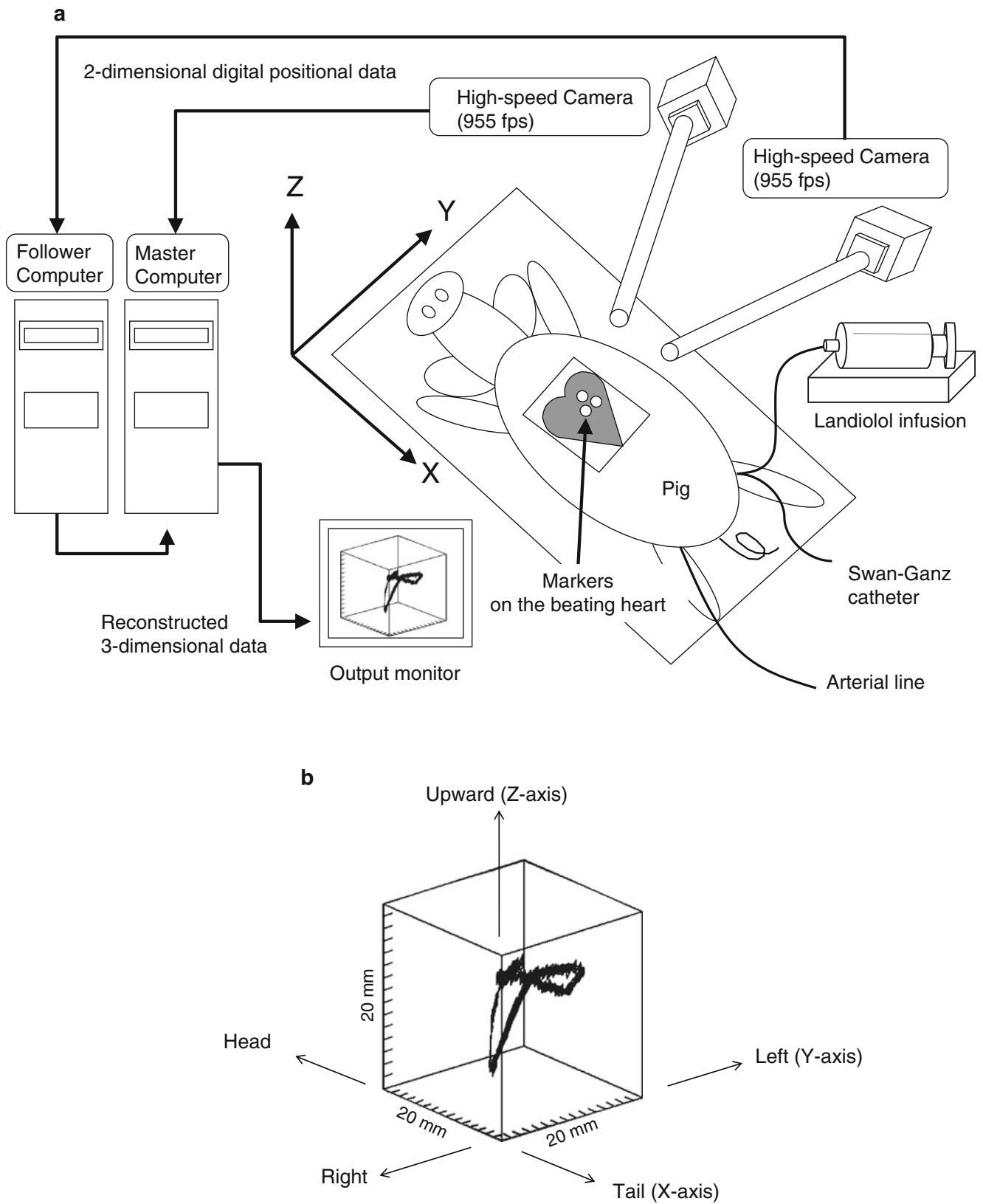


Fig. 10.4 (a) Three-dimensional digital motion capture and reconstruction system. Two high-speed cameras lining in a different angle capture the motion of markers on the beating heart. These 2-dimensional

position data of the surface of the coronary artery are reconstructed into 3-dimensional data in the master computer. (b) An example of 3-dimensional coronary artery motion in one cardiac cycle

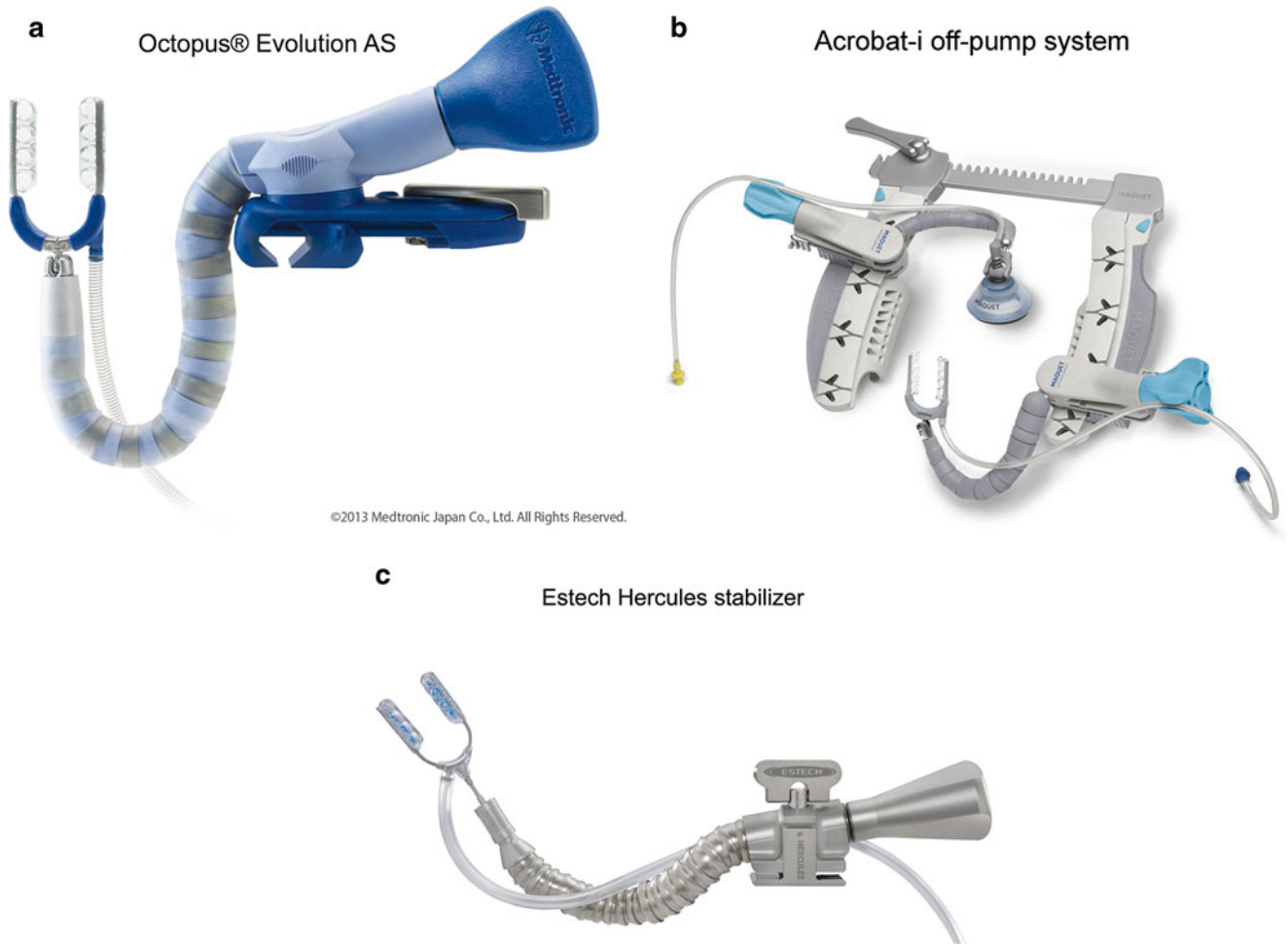
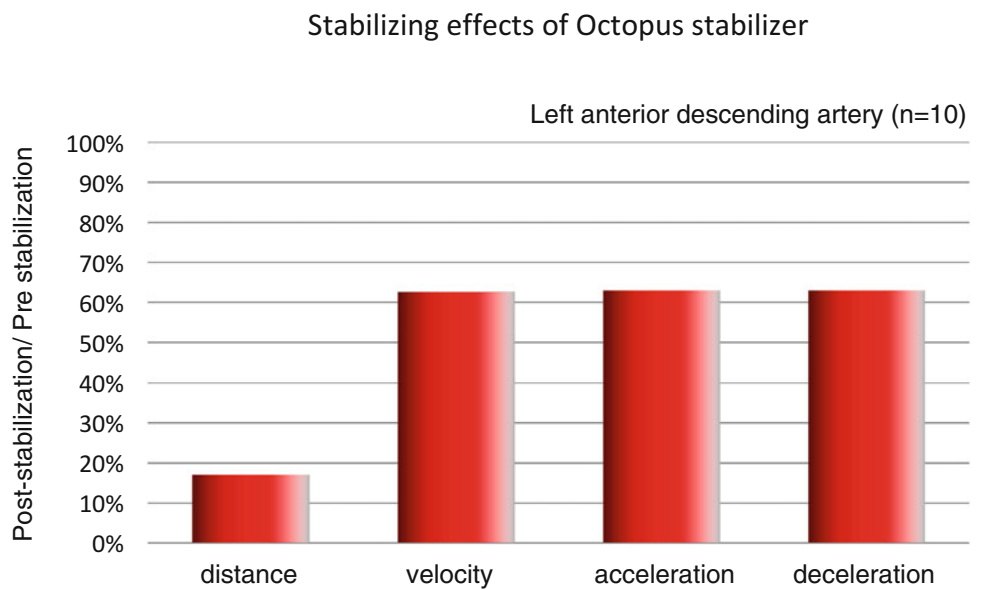


Fig. 10.5 Modern suction-type tissue stabilizers on the market. (a) Medtronic Octopus Evolution AS. (b) CTS Acrobat-i Off-Pump System. (c) Estech Hercules stabilizer

Fig. 10.6 Stabilization effect of Octopus (Modified from Ref. [7])



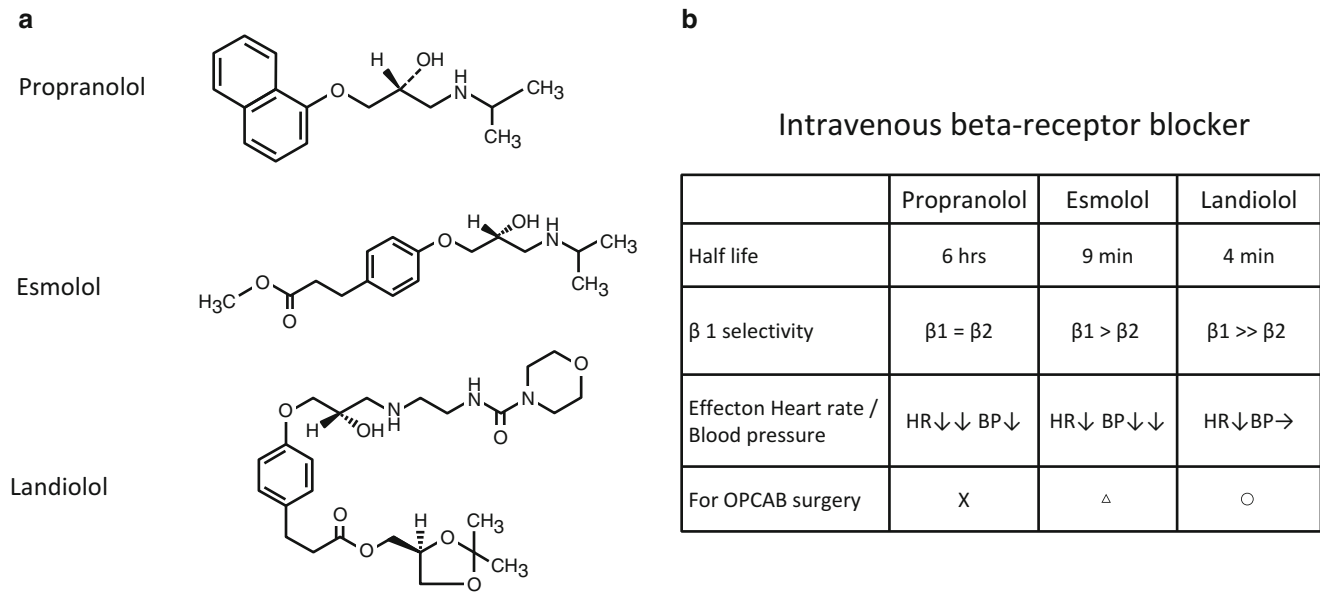


Fig. 10.7 Beta-blockers for intravenous administration. (a) Chemical structure. (b) Comparison of beta-blockers: propranolol has a long half-life that makes this drug uncontrollable during surgery. While esmolol decreases systemic blood pressure rather than heart rate, landiolol

decreases heart rate with sustained systemic blood pressure, which is a characteristic of this drug that makes it suitable for use in off-pump coronary artery bypass (OPCAB)

contraction force (negative inotropic effect), whereas β_2 -receptor blockers dilate the smooth muscle of blood vessels in the heart, brain, and other organs and contract the smooth muscle of the trachea. In the clinical settings, β -receptor blockers have been used for the patients with heart disease as antihypertensive, anti-arrhythmic, and antianginal agents. For the patients with ischemic heart disease, β_1 -receptor blockers also reduced myocardial damage in acute myocardial ischemia since they reduce myocardial metabolic requirements during ischemia and increase oxygen delivery to the ischemic myocardium during and after ischemia [14–17]. A recent study demonstrated that coronary anastomosis time during off-pump coronary artery bypass was shorter under an infusion of esmolol, a short-acting β_1 -blocker, suggesting favorable stabilization during β_1 -blocker infusion [17].

Propranolol (Fig. 10.7), a nonselective β_1 - and β_2 -receptor blocker, was first introduced as an anti-tachycardia and anti-tachyarrhythmia drug during coronary artery bypass surgery. However, propranolol has a long duration of action time (2–14 h) with several side effects such as conduction disturbance, hypotension, and cardiac failure [14, 15]. Propranolol also blocks β_2 -receptor with a risk of perioperative asthma attacks. Esmolol (Fig. 10.7), an ultra-short-acting selective β_1 -receptor blocker, has been developed recently to avoid these side effects [14, 15]. More recently, landiolol hydrochloride (Fig. 10.7) has been developed by modifying the chemical structure of esmolol, to increase β_1 -receptor selectivity and potency without affecting the duration of action.

This agent has some unique characteristics. Landiolol hydrochloride has a very rapid onset and offset of action [14–16, 18, 19]. Compared with esmolol, heart rate decreases more rapidly with landiolol [15–18]. Landiolol is rapidly metabolized by serum pseudocholinesterase and liver carboxylesterase to an inactive metabolite in humans within a half-life of 4 min, which is shorter than that of esmolol [14, 16, 18–20]. Renal and hepatic clearance does not contribute to the pharmacokinetics of this agent at clinical concentrations [18–20] which is useful for intraoperative infusion for the patients with renal and/or hepatic dysfunction [20]. Landiolol hydrochloride has higher β_1 -selectivity than any other known β -blocker [19]. It also suppresses ventricular and supraventricular arrhythmias in experimental settings [18, 19]. Furthermore, landiolol does not produce the dose-dependent decrease in mean arterial pressure like esmolol [15, 19], which seems to be suitable for off-pump coronary artery bypass surgery.

Landiolol, as a β_1 -blocker with negative inotropic effect, decreases the myocardial contractility or, in other words, decreases the developed force and velocity of myocardial contraction [21]. Because coronary artery sits on the contracting myocardium, there is a hypothesis that landiolol has an effect of cardiac motion stabilization during off-pump coronary artery bypass surgery.

Recently, Wakamatsu and associates [22] demonstrated that landiolol infusion achieves better stabilization of the surface coronary artery under the mechanical stabilizer on the beating heart (Fig. 10.8a). Landiolol decreases all motion

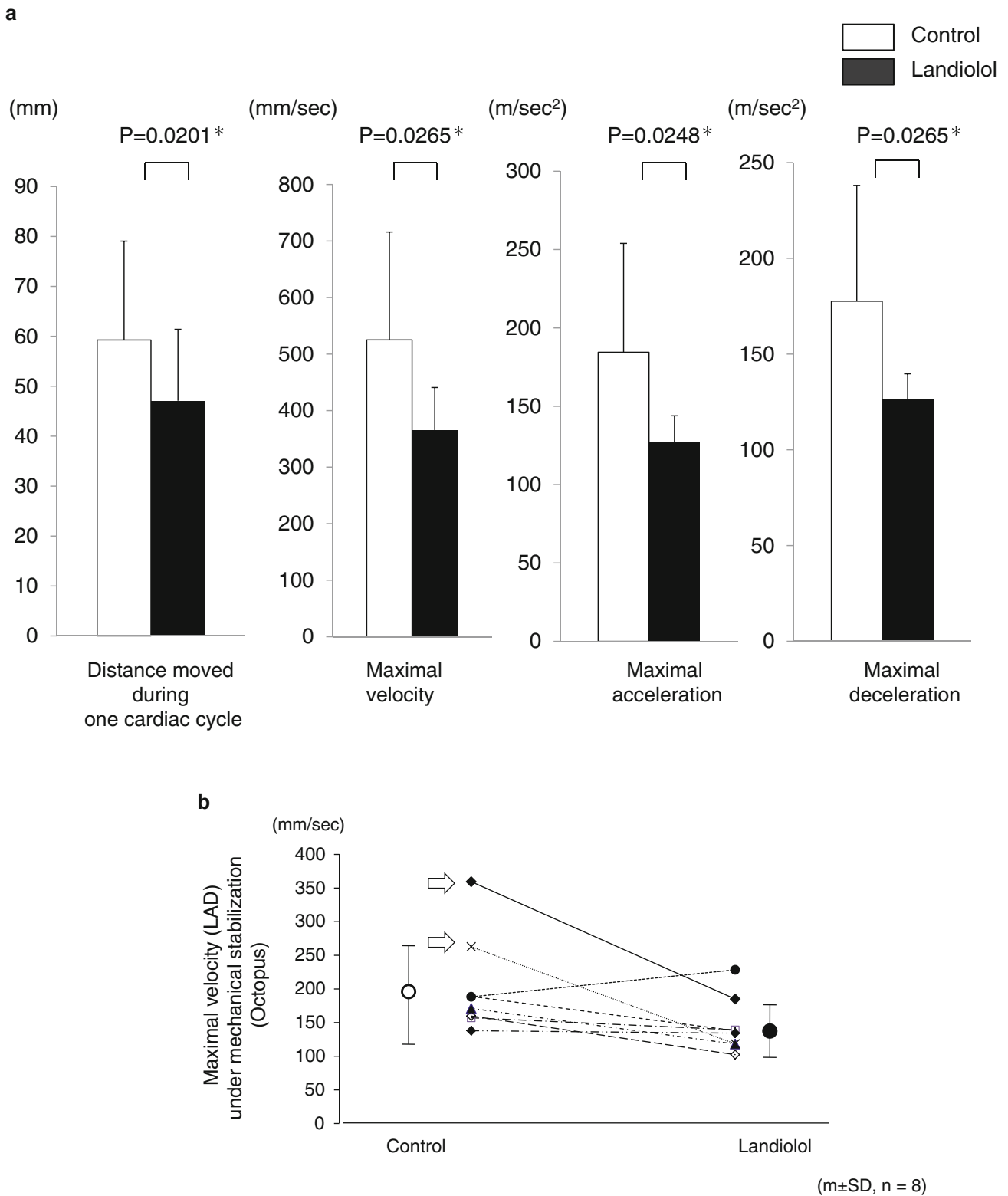


Fig. 10.8 Stabilization by beta-blocker. (a) Changes in motion parameters by intravenous infusion of landiolol hydrochloride. (b) Changes in maximal velocity by intravenous infusion of landiolol under mechanical stabilization. Note the point of poor stabilization (open arrow) which was stabilized by landiolol infusion

parameters, such as distance moved during one cardiac cycle, velocity, and acceleration/deceleration, at anastomosis site of the left anterior descending artery, left circumflex artery, and distal right coronary artery. These motion parameters were decreased by 20–30 %, in general, below the control level during landiolol infusion in the dose range with 10–15 % reduction in the heart rate and maintained systemic blood pressure.

As pointed out, sudden quick motion of the anastomosis site remains under mechanical stabilization, which obviously increases the surgical difficulty. Mechanical stabilizers also have a considerable deviation of the stabilizing effects depending on the individual variations of the coronary artery anatomy and periarterial fat deposition. For example, each data point under the mechanical stabilization showed considerable variation in maximal velocity (Fig. 10.8b). Landiolol infusion effectively decreased the maximal velocity, especially when this parameter was greater than the mean value or “poor stabilization” (Fig. 10.8b; open arrow). Thus, administration of landiolol hydrochloride can decrease the residual motion that remained after the application of mechanical stabilizer. Because β_1 -blockade has a negative inotropic action on the whole heart, landiolol exerts a general stabilization effect on the coronary arteries in any part of the beating heart, in addition to the local immobilization effect by mechanical stabilizer.

In conclusion, landiolol infusion during off-pump coronary artery bypass surgery is recommended to construct precise coronary artery anastomosis on the beating heart. Given a certain dose range of landiolol that decreases the heart rate but not the systemic blood pressure, the motion stabilization effect can be induced during beating heart surgery. Especially, landiolol infusion is recommended when the surgeon encounters unfavorable situations that the conventional mechanical stabilization only achieves a poor local stabilization because of individual anatomy variations in the specific target coronary arteries.

Dose and mode of landiolol administration should be carefully selected, because hypotension caused by cardiac manipulation or dislocation should be avoided during off-pump coronary artery bypass surgery. Yoshida and associates conducted clinical study of landiolol in the intensive care unit and recommended intravenous continuous infusion, not bolus administration, to avoid unexpected severe bradycardia or profound hypotension [23]. Our protocol of intraoperative landiolol infusion is as follows: after intratracheal intubation under general anesthesia, the continuous intravenous infusion of landiolol hydrochloride in very low dose (1 $\mu\text{g}/\text{kg}/\text{min}$) is started. During sternotomy and graft harvesting, the dose of landiolol increased gradually as long as systemic blood pressure is maintained as high as the preoperative value. The infusion is continued over night and

stopped gradually after the patient starts to take oral beta-blocker. As the result, the dose of landiolol is low (average 3–5 $\mu\text{g}/\text{kg}/\text{min}$; range 1–20 $\mu\text{g}/\text{kg}/\text{min}$) without serious side effects such as severe hypotension or bradycardia. In addition to the stabilizing effect of the coronary anastomosis site, recent clinical study demonstrates that this protocol prevents postoperative atrial fibrillation [24].

10.5 Other Factors Affecting the Stabilization

10.5.1 Vasopressors

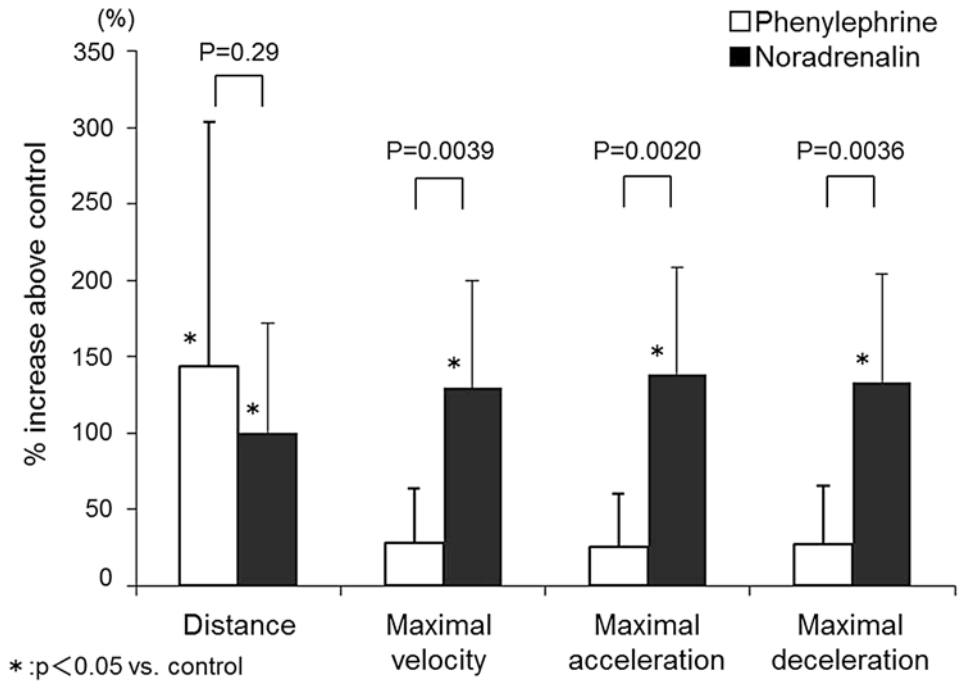
Hemodynamic collapse or systemic hypotension may occur as an adverse event during off-pump coronary artery bypass surgery. Hemodynamic variations can be caused by several factors, including (1) displacement and (2) stabilization of the heart, as well as (3) myocardial ischemia during coronary occlusion [25]. Vertical displacement of the heart to access the lateral and inferior walls decreases the venous return, stroke volume, cardiac index, and mean arterial pressure [26, 27].

Under these circumstances, the hypotension is tentatively treated with intravenous administration of vasopressors such as noradrenaline or phenylephrine by anesthesiologists. Noradrenaline is a potent α_1 - and β_1 -receptor agonist, with minor effects on β_2 -receptors; thus it increases the blood pressure by increasing the cardiac output and systemic vascular resistance [28]. Phenylephrine is a synthetic, selective α_1 -adrenergic receptor agonist that increases the blood pressure by increasing the peripheral vascular resistance with either no change or a decrease in the cardiac output [29, 30].

Recently, Kurosawa and associates [31] found that an infusion of noradrenaline significantly increases the target coronary artery motion under mechanical stabilization on a beating heart, whereas phenylephrine does not (Fig. 10.9). The administration of noradrenaline, at the dose required to increase the systolic arterial pressure by 30–50 %, significantly increased all motion parameters at the anastomosis site on the left anterior descending artery. In contrast, the administration of phenylephrine at the dose required to increase the systolic arterial pressure by 30–50 % did not significantly increase the 3-dimensional cardiac motion parameters, except for the distance moved during one cardiac cycle at the anastomosis site on the left anterior descending artery.

In conclusion, the use of a vasopressor with little influence on the coronary artery motion is recommended for the anesthesiologists in the need for maintenance of systemic blood pressure during off-pump coronary artery bypass surgery.

Fig. 10.9 Comparison of noradrenaline and phenylephrine on coronary artery motion



Frank-Starling curve

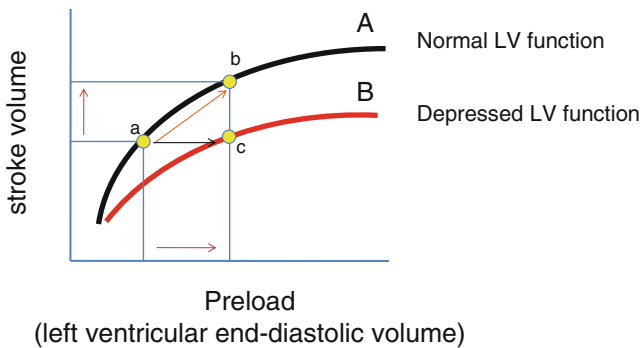


Fig. 10.10 Frank-Starling curve. In the normal functioning heart (A), decreased heart rate increases the preload and stroke volume (a → b). In the heart with depressed contractile function (B), decreased heart rate only increases the preload, not the stroke volume (a → c)

10.5.2 Heart Pacing

Heart pacing during off-pump coronary artery is recommended by two reasons: (1) increased cardiac output and (2) decreased coronary artery motion.

Frank-Starling's Law shows that the cardiac preload determines the cardiac output (Fig. 10.10). When the cardiac function is normal (Fig. 10.10; [A]), bradycardia elongates the diastolic phase of the heart, increasing the left ventricular end-diastolic volume (preload) and stroke volume as well, without a decrease in the cardiac output. However, when cardiac function is depressed (Fig. 10.10;

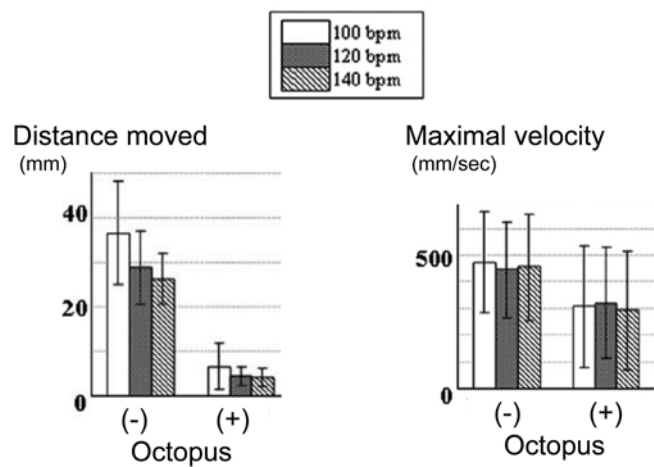


Fig. 10.11 Effect of cardiac pacing on coronary artery motion

[B]), bradycardia only increased the left ventricular end-diastolic volume and pressure, but not the stroke volume, resulting in the failing heart with excessive preload. To avoid these critical conditions of the depressed heart, maintenance of the heart rate by an intraoperative pacing is recommended either by atrial or ventricular lead or Swan-Ganz pacing.

Figure 10.11 shows the stabilizing effect of heart pacing. When the heart rate is increased by pacing, the distance moved during one cardiac cycle is decreased [7]. There is an explanation for this phenomenon. Again by the Frank-Starling's Law, increased heart rate decreases stroke volume by shortening the diastolic phase of the left ventricle. Decreased stroke volume represents a decreased maximal

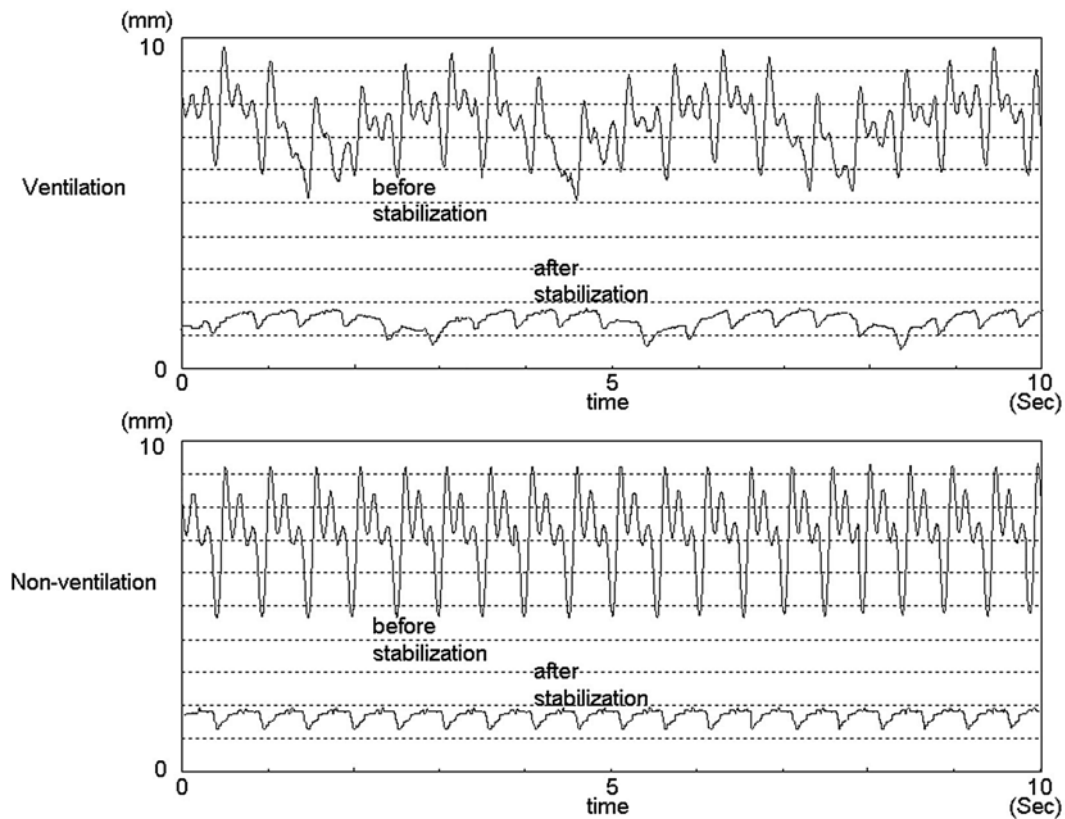


Fig. 10.12 A trace of coronary artery motion on the beating heart with or without mechanical lung ventilation

myocardial contraction, which influences the coronary artery sitting just above the myocardium.

The author recommends pacing the heart to maintain the heart rate above 80 beats /min especially when the surgeon encounters the heart with depressed cardiac function and bradycardia during off-pump surgery.

10.5.3 Mechanical Ventilation

The heart is adjacent to the bilateral lungs. The lung motion or lung ventilation affects the heart position. Cattin [5] demonstrated displacement of the heart by positive-pressure ventilation by high-speed camera. Lemmma [6], by

3-dimensional motion analysis, pointed out that positive-pressure ventilation has an important influence on cardiac surface stabilization. As shown in Fig. 10.12, the coronary artery motion is influenced by mechanical ventilation in low-frequency motion pattern even under the mechanical stabilization [7]. The heart is displaced in a tidal volume-dependent manner [32] (Fig. 10.13).

Here is a tip for mechanical ventilation during coronary artery anastomosis in off-pump coronary artery bypass surgery. A low tidal volume, high-frequency mechanical ventilation is recommended to the anesthesiologist if appropriate. Another tip is a short-time (few seconds) cessation of the mechanical ventilation when the surgeon is just trying a technically demanding stitch on the fine coronary artery wall (Fig. 10.14).

Fig. 10.13 Savitzky-Golay smoothing filter separates the motion of the coronary artery into cardiac contraction-generated motion and ventilation-generated motion

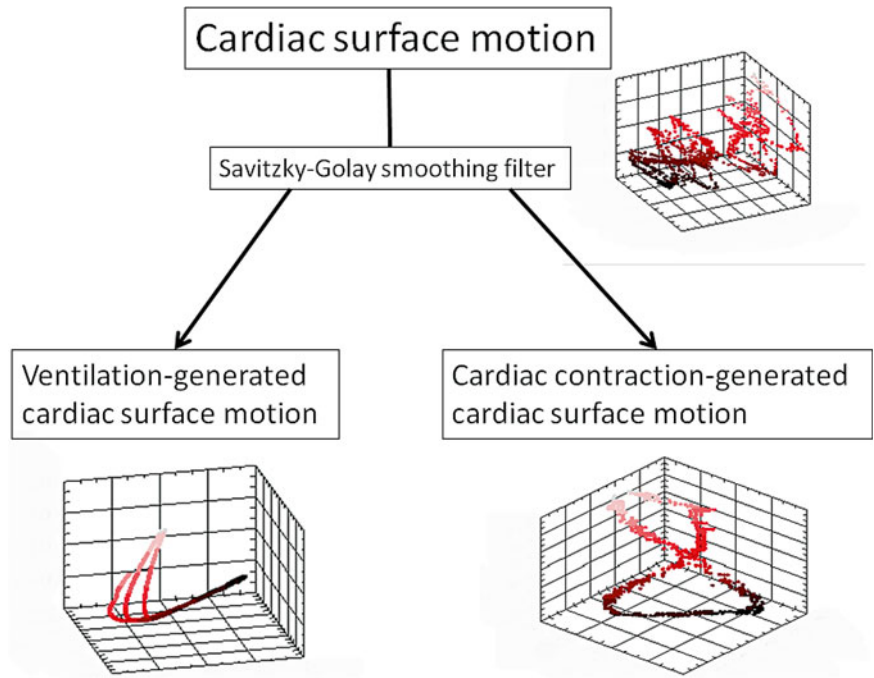
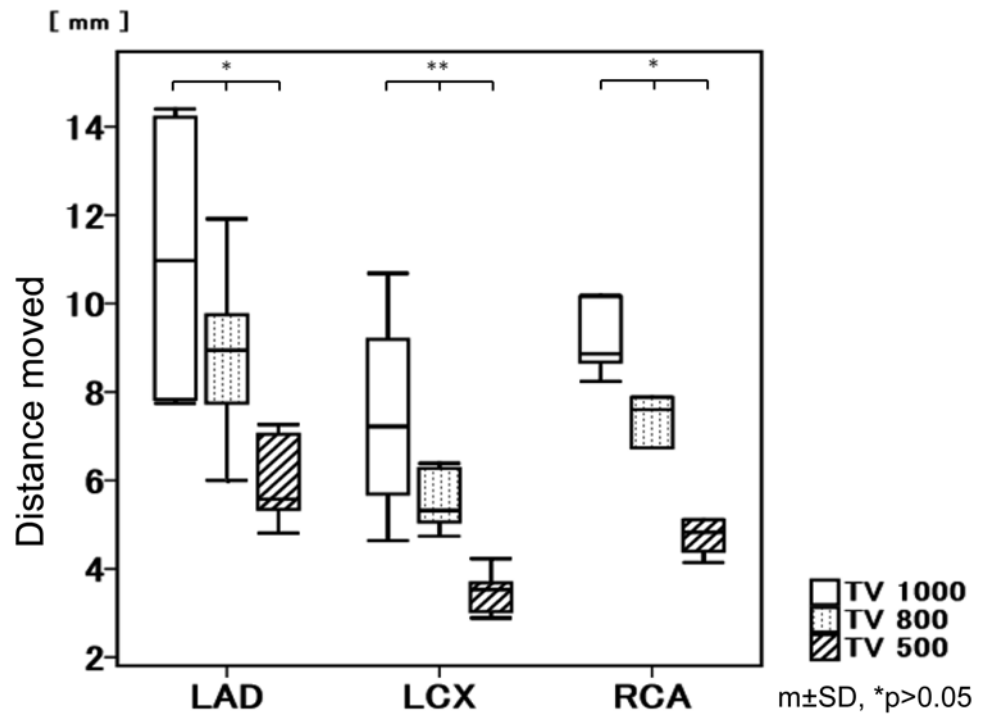


Fig. 10.14 The coronary artery is displaced in a ventilation volume-dependent manner



References

- Taylor R, Jensen P, Whitcomb L, Barnes A, Kumar R, Stoianovici D, Kavoussi L (1999) A steady-hand robotic system for microsurgical augmentation. *Int J Robot Res* 18(12):1201–1210
- Borst C, Jansen EW, Tulleken CA, Grundeman PF, Mansvelt Beck HJ, van Dongen JW, Bredée JJ (1996) Coronary artery bypass grafting without cardiopulmonary bypass and without interruption of native coronary flow using a novel anastomosis site restraining device (“Octopus”). *J Am Coll Cardiol* 27(6):1356–1364
- Detter C, Deuse T, Christ F, Boehm DH, Reichenspurner H, Reichart B (2002) Comparison of two stabilizer concepts for off-pump coronary artery bypass grafting. *Ann Thorac Surg* 74(2):497–501
- Koransky ML, Tavara ML, Yamaguchi A, Kown MH, Miniati DN, Nowlin W, Robbins RC (2003) Quantification of mechanical stabilization for the performance of off-pump coronary artery surgery. In: *The heart surgery forum*, vol 6, no. 4. Carden Jennings Publishing Co, Charlottesville, pp 224–231
- Cattin P, Dave H, Grünenfelder J, Szekely G, Turina M, Zünd G (2004) Trajectory of coronary motion and its significance in robotic motion cancellation. *Eur J Cardiothorac Surg* 25(5):786–790
- Lemma M, Mangini A, Redaelli A, Acocella F (2005) Do cardiac stabilizers really stabilize? Experimental quantitative analysis of mechanical stabilization. *Interact Cardiovasc Thorac Surg* 4(3):222–226
- Watanabe T, Omata S, Odamura M, Okada M, Nakamura Y, Yokoyama H (2006) Three-dimensional quantification of cardiac surface motion: a newly developed three-dimensional digital motion-capture and reconstruction system for beating heart surgery. *J Thorac Cardiovasc Surg* 132(5):1162–1171
- Buffolo EJC, Andrade JCS, Branco JNR, Aguiar LF, Ribeiro EE, Jatene AD (1990) Myocardial revascularization without extracorporeal circulation. *Eur J Cardiothorac Surg* 4(9):504–508
- Benetti FJ, Naselli G, Wood M, Geffner L (1991) Direct myocardial revascularization without extracorporeal circulation. Experience in 700 patients. *CHEST J* 100(2):312–316
- Pfister AJ, Zaki MS, Garcia JM, Mispireta LA, Corso PJ, Qazi AG, Gurny P (1992) Coronary artery bypass without cardiopulmonary bypass. *Ann Thorac Surg* 54(6):1085–1092
- Fanning WJ, Kakos GS, Williams TE (1993) Reoperative coronary artery bypass grafting without cardiopulmonary bypass. *Ann Thorac Surg* 55(2):486–489
- Mohr R, Moshkovitz Y, Agranat O (1993) Coronary artery bypass without cardiopulmonary bypass: low-risk surgery for high-risk patients [abstract]. *Circulation* 88:I-637
- Jansen EW, Grundeman PF, Borst C, Eefting F, Diephuis J, Nierich A, Cotrufo M (1997) Less invasive off-pump CABG using a suction device for immobilization: the ‘Octopus’ method. *Eur J Cardiothorac Surg* 12(3):406–412
- Ahmet I, Fukushima N, Sawa Y, Masai T, Kadoba K, Kagisaki K et al (1999) The effect of a new ultra-short-acting beta-adrenergic blocker, ONO-1101, on cardiac function during and after cardiopulmonary bypass. *Surg Today* 29:248–254
- Sasao J, Tarver SD, Kindscher JD, Taneyama C, Benson KT, Goto H (2001) In rabbits, landiolol, a new ultra-short-acting β -blocker, exerts a more potent negative chronotropic effect and less effect on blood pressure than esmolol. *Can J Anesth* 48:985–989
- Bessho R, Chambers DJ (2001) Myocardial protection: the efficacy of an ultra-short-acting β -blocker, esmolol, as a cardioplegic agent. *J Thorac Cardiovasc Surg* 122(5):993–1003
- Otaki M, Ogawa T, Inoue T, Oku H (2002) Off-pump coronary bypass grafting to double vessel disease with the pharmacological assist of esmolol: an experimental study. *J Cardiovasc Surg* 43(3):307–311
- Atarashi H, Kuruma A, Yashima MA, Saitoh H, Ino T, Endoh Y, Hayakawa H (2000) Pharmacokinetics of landiolol hydrochloride, a new ultra-short-acting β -blocker, in patients with cardiac arrhythmias. *Clin Pharm Therap* 68(2):143–150
- Sugiyama A, Takahara A, Hashimoto K (1999) Electrophysiologic, Cardiohemodynamic and [beta]-blocking actions of a new ultra-short-acting [beta]-blocker, ONO-1101, assessed by the in vivo canine model in comparison with esmolol. *J Cardiovasc Pharmacol* 34(1):70–77
- Takahata T, Yasui-Furukori N, Sakamoto J, Suto K, Suto T, Tateishi T, Munakata A (2005) Influence of hepatic impairment on the pharmacokinetics and pharmacodynamics of landiolol hydrochloride, an ultra-short-acting β 1-blocker. *Drugs R & D* 6(6):385–394
- Levy MN, Pappano AJ, Berne RM (2007) *Cardiovascular physiology*. Mosby Elsevier, Philadelphia
- Wakamatsu H, Watanabe T, Sato Y, Takase S, Omata S, Yokoyama H (2010) Selective beta-1 receptor blockade further reduces the mechanically stabilized target coronary artery motion during beating heart surgery. *Innov Technol Tech Cardiothorac Vasc Surg* 5(5):349–354
- Yoshida Y, Terajima K, Sato C, Akada S, Miyagi Y, Hongo T, ... Sakamoto A (2008) Clinical role and efficacy of landiolol in the intensive care unit. *J Anesth* 22(1):64–69
- Wakamatsu H, Yokoyama H (2011) Intraoperative infusion of landiolol hydrochloride, an ultra-short acting beta-1 adrenergic receptor blocker, prevents postoperative atrial fibrillation after off-pump coronary artery bypass surgery. *CHEST J* 140(4_MeetingAbstracts):508A–508A
- Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, ... Novitzky D (2009) Veterans affairs Randomized On/Off Bypass (ROOBY) Study Group. On-pump versus off-pump coronary-artery bypass surgery. *N Engl J Med* 361(19):1827–1837
- Couture P, Denault A, Limoges P, Sheridan P, Babin D, Cartier R (2002) Mechanisms of hemodynamic changes during off-pump coronary artery bypass surgery. *Can J Anesth* 49(8):835–849
- Mishra M, Malhotra R, Mishra A, Meharwal ZS, Trehan N (2002) Hemodynamic changes during displacement of the beating heart using epicardial stabilization for off-pump coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth* 16(6):685–690
- Schwarz B, Hofstötter H, Salak N, Pajk W, Knotzer H, Mayr A, ... Hasibeder W (2001) Effects of norepinephrine and phenylephrine on intestinal oxygen supply and mucosal tissue oxygen tension. *Intens Care Med* 27(3):593–601
- Klaus S, James R (1981) Alpha1- and alpha2-adrenoceptors: pharmacology and clinical implications. *J Cardiovasc Pharmacol* 3(Suppl 1):S14–S23
- Dunaway S, Yu Q, Larson DF (2007) Effect of acute alpha adrenergic stimulation on cardiac function. *Perfusion* 22(4):289–292
- Kurosawa H, Seto Y, Wakamatsu H, Sato Y, Takase S, Omata S, Yokoyama H (2014) Effects of phenylephrine and noradrenaline on coronary artery motion in an open-chest porcine beating heart model. *Surg Today* 44:1128–1137
- Sato Y, Yokoyama H Intraoperative mechanical ventilation affects cardiac surface motion during beating heart surgery (in submission)