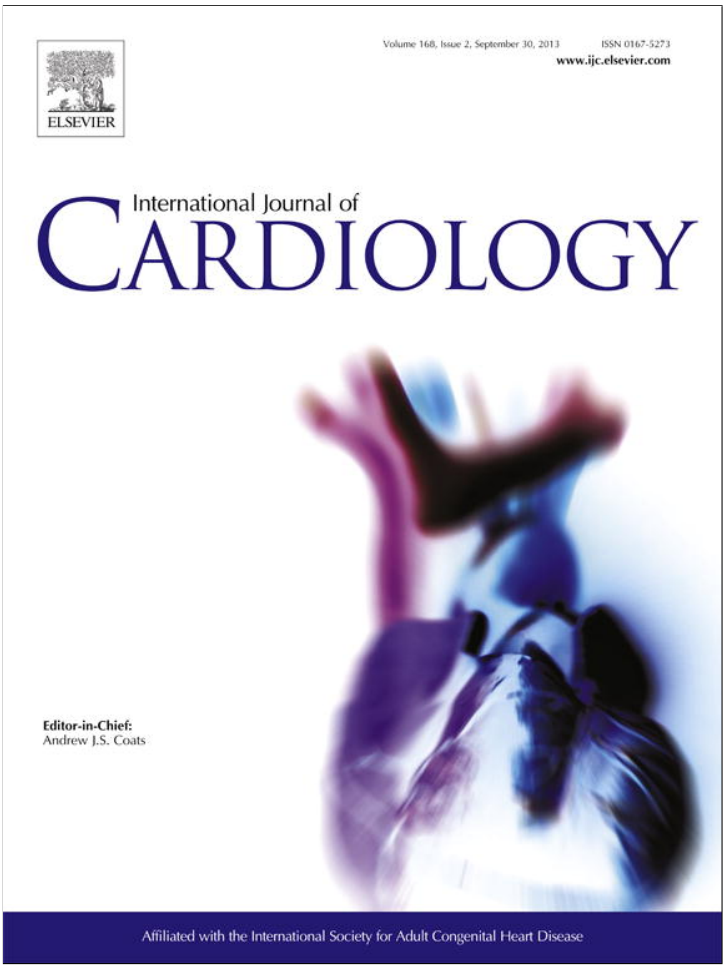

collaboration with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol 2007;49:378–402.
[5] Sarwar A, Shaw LJ, Shapiro MD, et al. Diagnostic and prognostic value of absence of coronary artery calcification. JACC Cardiovasc Imaging 2009;2:675–88.
[6] Mieres JH, Makaryus AN, Redberg RF, Shaw LJ. Noninvasive cardiac imaging. Am Fam Physician 2007;75:1219–28.
[7] Nicoll R, Henein MY. Calcific cardiac disease: a comprehensive investigation into its true nature. Int J Cardiol 2010;145:599–600.
[8] Rennenberg RJ, Kessels AG, Schurgers LJ, van Engelshoven JM, de Leeuw PW, Kroon AA. Vascular calcifications as a marker of increased cardiovascular risk: a meta-analysis. Vasc Health Risk Manag 2009;5:185–97.
[9] Nieman K, Galema TW, Neefjes LA, et al. Comparison of the value of coronary calcium detection to computed tomographic angiography and exercise testing in patients with chest pain. Am J Cardiol 2009;104:1499–504.
[10] Bartel AG, Behar VS, Peter RH, Orgain ES, Kong Y. Graded exercise stress tests in angiographically documented coronary artery disease. Circulation 1974;49:348–56.

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Exercise training and obesity in Italian children directly assessed by primary school teachers with tele-cardiology support: A pilot experience

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Worldwide prevalence of childhood obesity has increased greatly during the past three decades [1]. The prevalence doubled or trebled between the early 1970's and late 1990's in several countries [2]. It was predicted that by 2010, over 38–40% of children in the North American and European regions would be overweight/obese.

Preventive strategies aimed at reduction of global burden of future obesity should therefore be undertaken very early, possibly starting in childhood or adolescence. School health programs should focus on early identification of children with an impaired exercise training and obesity.

Tele-medicine support is presently applied in several fields of medicine [3–12]; tele-cardiology was shown useful in the management of acute coronary syndrome [13,14], atrial fibrillation [15], syncope [16] and even in implementing strategies of cardiovascular primary care [17]. Tele-medicine support allows "lay" non-medical individuals to deliver medical acts which should be usually done by health-care professionals [18].

We therefore aimed to report on the feasibility and preliminary findings of a pilot experience which evaluated exercise training and obesity in Italian children directly assessed by primary school teachers with tele-cardiology support.

Forty consecutive children attending either 4th or 5th class in an Italian primary school (in Manfredonia, Apulia, Italy) were enrolled in the study. All participants underwent tele-cardiology ECG registration by tele-medicine support at rest (T_1) and 2 min after exercise (30 min volleyball match) (T_2).

The ECG was recorded by a school teacher who previously attended a 1-hour training in order to acquire the skills needed to record an ECG with a pocket ECG-recorder (Cardiovox P12). The ECGs were sent by telephone connection to a regional tele-cardiology "hub" serving the entire region Apulia, located in Bari, more than 100 km far from Manfredonia, where the primary school was situated. Tele-medicine support was provided by Cardio-on-Line Europe s.r.l. (Bari, Italy) as previously described elsewhere [19]; a cardiologist available 24/7 within tele-cardiology hub promptly read the ECGs which were immediately sent back via the internet, fax or visualized back on smart-phones. The tele-cardiology hub also supports the local emergency medical service 118 Apulia.

Gender, height, weight, waist circumference were also recorded and body mass index (BMI) was calculated and plotted on CDC growth charts for male and female children and adolescents in order to define the grade of obesity.

The study was authorized by local supervisory education authorities.

Continuous variables were expressed as mean ± standard deviation and compared with Student's t-test for unpaired or paired groups as required and dichotomic variables as percentages. Correlations were analyzed with Pearson's test. A p value <0.05 was considered as statistically significant.

Children's characteristics are given in Table 1 (Figs. 1–3). Twenty-three percent of population was overweight, 26% obese (Fig. 2). No differences were found among genders excluding height ($p < 0.05$).

Table 1
Population's characteristics.

	Mean	Std. dev.
Male gender	50.0%	
Age	9.1	0.5
Height	1.4	0.1
Weight	38.5	10.7
Basal heart rate (T_1)	97.2	12.0
Heart rate after exercise (T_2)	132.1	16.9
T_2–T_1 difference	33.8	18.0
Body mass index	19.1	3.9
Waist circumference	68.0	8.2

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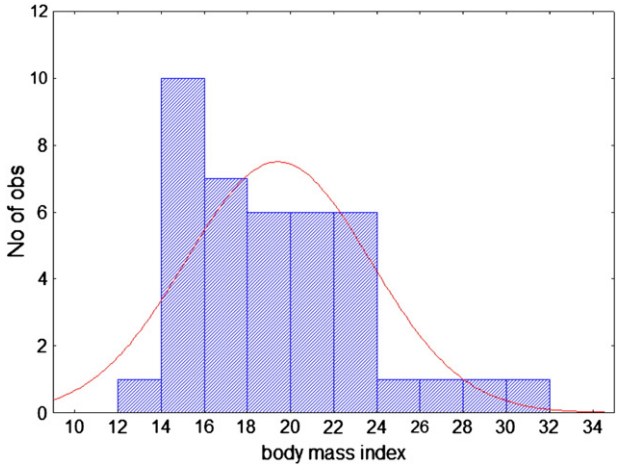

Fig. 1. Body mass index distribution.

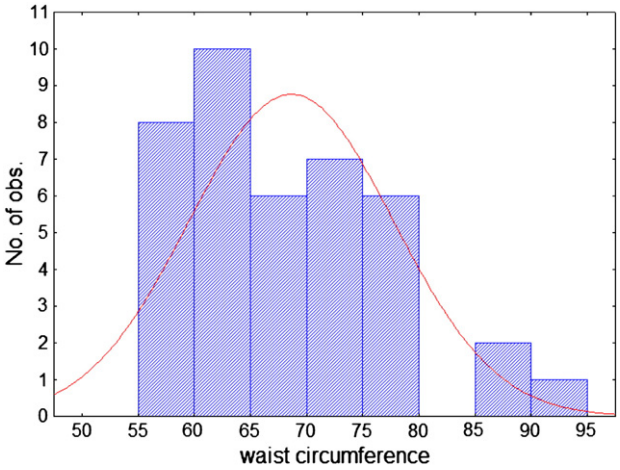

Fig. 3. Waist circumference.

Electrocardiograms were normal with sinus rhythm in all cases; only one case of supraventricular premature contractions was found. Heart rate rose from a mean value of 97 ± 13 (T_1) to 132 ± 17 bpm (T_2) after exercise ($p < 0.001$) (Fig. 4).

Heart rate values after exercise were related to body mass index (r 0.34, $p < 0.05$) (Fig. 5) and waist circumference (r 0.33, $p < 0.05$) (Fig. 6).

We showed in this report the preliminary findings of a pilot experience which evaluated exercise training and obesity in Italian children directly assessed by primary school teachers with tele-cardiology support. The ECG assessment was easily performed by "lay" individuals after a short training. To best of our knowledge these are among the first data on school health programs with "lay" individuals and tele-medicine support. Most data on tele-medicine for childhood health come from study assessing the feasibility of remote echocardiography consultation in case of suspected congenital heart disease [20,21]. Few data instead are available on tele-medicine implementation in other childhood contexts [22,23].

The prevalence of overweight/obesity was found rather high, in line with prior reports also coming from Italian populations; in a region-wide registry from Tuscany, Italy, the prevalence of overweight (including obesity) ranged 32–33% in children aged 9 in 2006 [24]. The pediatric obesity continues to rise in parallel with increases in incidence of pediatric type 2 diabetes [25] and insulin resistance in adolescents with type-2 diabetes is associated with impaired exercise capacity [26].

Among 1003 sixth graders (average age 11.5 years) in the mid-west of USA 15% were obese; obese students had higher levels of total cholesterol, low-density lipoprotein cholesterol, triglycerides, blood pressure, and recovery heart rates [27]. They consumed more regular soda and school lunches but were less likely to engage in physical activities. Obese students were more likely to watch television ≥2 h per day.

We also showed as low exercise training in terms of higher heart rates 2 min after exercise is related to clinical markers of obesity such as higher body mass index and waist circumference. Data from the Framingham study documented as resting heart rate is a prognostic marker for long term cardiovascular outcomes in adults [28]. In a recent study, resting heart rate was positively linked in 14,842 children aged 6–18 years to waist circumference, and blood pressure, and negatively associated with age and exercise frequency [29]. Also body mass index, however, is related to long term mortality [30].

Low physical activity was associated with "fat" body-composition indexes in children aged 6–8 years at varied risk of obesity [31]. Obese adolescent boys with metabolic syndrome show low physical performance [32]. In children at risk of obesity physical activity levels were positively associated with lean mass index and negatively associated with fat mass index but not with body mass index [31]. Obese subjects have a marked impairment of heart rate behavior during exercise and in the recovery period, and the blunted increase in heart rate is the most important factor that influences exercise capacity [33]. Peak heart rate, heart rate recovery and chronotropic index are lower in obese subjects,

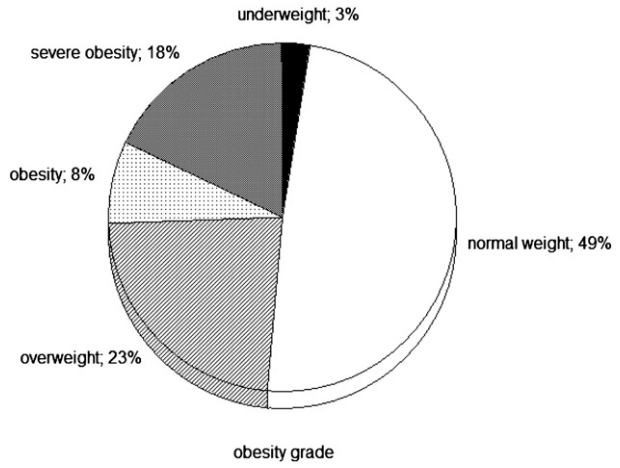

Fig. 2. Weight characteristics.

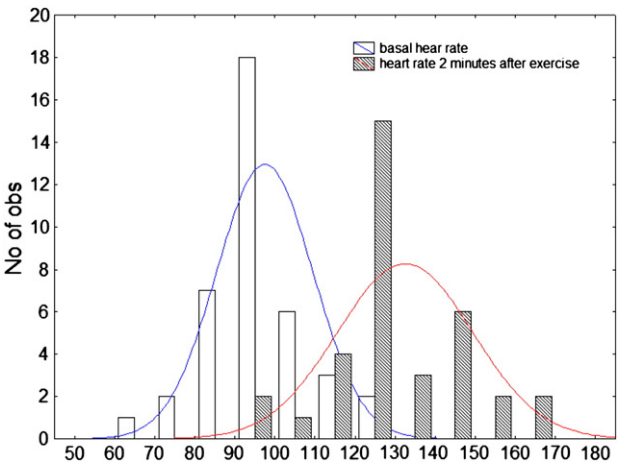

Fig. 4. Heart rate before and after exercise.

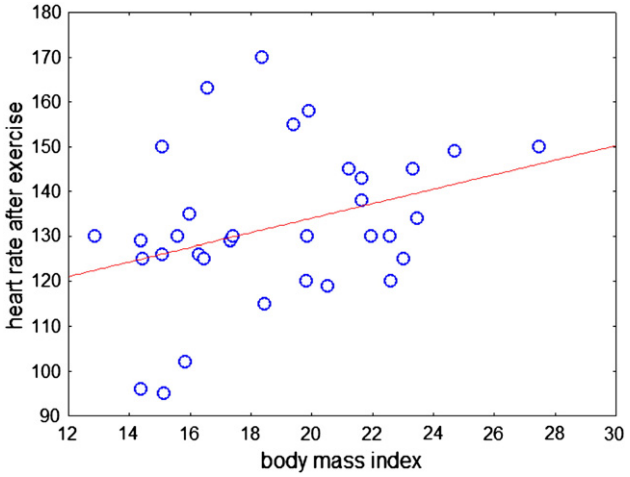

Fig. 5. Correlation between body mass index and heart rate after exercise.

regardless of their fitness level. In children 9 to 11 years of age fasting insulin concentration is associated with cardiovascular reactivity to exercise [34].

Even impaired exercise capacity expresses as lower heart rate recovery is related to both obesity and cardiovascular risk. Impaired exercise capacity was related to increased body weight in several studies. Heart rate recovery is associated with obesity traits and related cardio-metabolic risk factors in children and adolescents [35]. There is an inverse correlation between heart rate recovery and metabolic risks in healthy children and adolescents [36]. Heart rate reserve was shown as a predictor of cardiovascular and all-cause mortality in men [37]. The risk of mortality was more than twice in subjects with low heart rate recovery [38]. Heart rate recovery following maximal exercise testing is a predictor of cardiovascular disease and all-cause mortality in men with diabetes [39]. Metabolic syndrome is associated with impaired heart rate recovery and low exercise capacity in young male adults [40], although weight loss improves heart rate recovery in overweight and obese men with features of the metabolic syndrome [41]. The improvement in heart rate recovery is significantly correlated with decreases in body weight, body mass index, waist circumference, plasma glucose, serum triglycerides, and triglyceride/high-density lipoprotein ratio.

Fortunately the implementation of school health program may reverse this negative relation between obesity and low physical activity. In obese children, 4 months of daily physical activity and cardiovascular fitness lowered percent body fat, total body fat mass and visceral adipose tissue and increased significantly fat-free mass [42]. Exercise alone

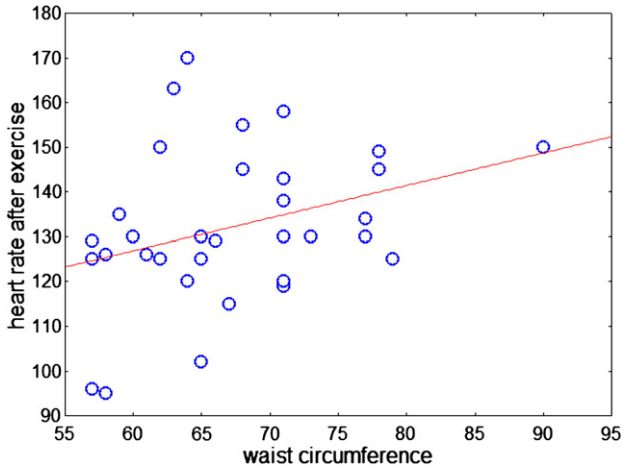

Fig. 6. Correlation between waist circumference and heart rate after exercise.

reduces insulin resistance in obese children independently of changes in body composition [43].

Tele-cardiology support may therefore be of help in implementing such programs for the future [44]; further studies however are needed to confirm these preliminary data on small population.

In conclusion, we report the preliminary findings of a pilot experience which evaluated exercise training and obesity in Italian children directly assessed by primary school teachers with tele-cardiology support. Heart rate after exercise values were related to obesity.

This is a preliminary non randomized study on very small population. The exercise protocol is not standardized and the workload is not exactly quantified.

References

[1] Han JC, Lawlor DA, Kimm SY. Childhood obesity. Lancet May 15 2010;375(9727):1737–48.
[2] Wang Y, Lobstein T. Worldwide trends in childhood overweight and obesity. Int J Pediatr Obes 2006;1:11–25.
[3] Wootton R. Twenty years of telemedicine in chronic disease management—an evidence synthesis. J Telemed Telecare 2012;18:211–20.
[4] de Waure C, Cadeddu C, Gualano MR, Ricciardi W. Telemedicine for the reduction of myocardial infarction mortality: a systematic review and a meta-analysis of published studies. Telemed J E Health 2012;18:323–8.
[5] Anker SD, Koehler F, Abraham WT. Telemedicine and remote management of patients with heart failure. Lancet 2011;378:731–9.
[6] Hailey D, Roine R, Ohinmaa A, Dennett L. Evidence of benefit from telerehabilitation in routine care: a systematic review. J Telemed Telecare 2011;17:281–7.
[7] Hasan A, Paul V. Telemonitoring in chronic heart failure. Eur Heart J 2011;32:1457–64.
[8] Polisena J, Tran K, Cimon K, et al. Home telemonitoring for congestive heart failure: a systematic review and meta-analysis. J Telemed Telecare 2010;16:68-7.
[9] Bartoli L, Zanaboni P, Masella C, Ursini N. Systematic review of telemedicine services for patients affected by chronic obstructive pulmonary disease (COPD). Telemed J E Health 2009;15:877–83.
[10] Schwamm LH, Holloway RG, Amarenco P, et al. A review of the evidence for the use of telemedicine within stroke systems of care: a scientific statement from the American Heart Association/American Stroke Association. Stroke 2009;40:2616–34.
[11] Keane MG. A review of the role of telemedicine in the accident and emergency department. J Telemed Telecare 2009;15:132–4.
[12] Ekeland AG, Bowes A, Flottorp S. Effectiveness of telemedicine: a systematic review of reviews. Int J Med Inform 2010;79:736–71.
[13] Brunetti ND, De Gennaro L, Amodio G, et al. Telecardiology applied to a region-wide public emergency health care service. J Thromb Thrombolysis 2009;28:23–30.
[14] Brunetti ND, De Gennaro L, Amodio G, et al. Telecardiology improves quality of diagnosis and reduces delay to treatment in elderly patients with acute myocardial infarction and atypical presentation. Eur J Cardiovasc Prev Rehabil 2010;2010(17):615–20.
[15] Brunetti ND, De Gennaro L, Pellegrino PL, Dellegrottaglie G, Antonelli G, Di Biase M. Atrial fibrillation with symptoms other than palpitations: incremental diagnostic sensitivity with at-home tele-cardiology assessment for emergency medical service. Eur J Cardiovasc Prev Rehabil 2012;19:306–13.
[16] Brunetti ND, De Gennaro L, Dellegrottaglie G, Antonelli A, Amoruso D, Di Biase M. Prevalence of cardiac arrhythmias in pre-hospital tele-cardiology electrocardiograms of emergency medical service patients referred for syncope. J Electrocardiol 2012;45:727–32.
[17] Brunetti ND, De Gennaro L, Dellegrottaglie G, et al. Rationale and design for a cardiovascular screening and prevention study with tele-cardiology in Mediterranean Italy: the CAPITAL study (CArdiovascular Prevention wIth Telecardiology in ApuLia). Int J Cardiol 2011;149:130–3.
[18] Ting HH, Krumholz HM, Bradley EH, et al. Implementation and integration of prehospital ECGs into systems of care for acute coronary syndrome: a scientific statement from the American Heart Association Interdisciplinary Council on Quality of Care and Outcomes Research, Emergency Cardiovascular Care Committee, Council on Cardiovascular Nursing, and Council on Clinical Cardiology. Circulation 2008;118:1066–79.
[19] Brunetti ND, De Gennaro L, Dellegrottaglie G, Amoruso D, Antonelli G, Di Biase M. A regional pre-hospital ECG network with a single tele-cardiology "hub" for public emergency medical service: technical requirements, logistics, manpower and preliminary results. Telemed J E Health 2011;17:727–33.
[20] McCrossan BA, Grant B, Morgan GJ, Sands AJ, Craig B, Casey FA. Diagnosis of congenital heart disease in neonates by videoconferencing: an eight-year experience. J Telemed Telecare 2008;14:137–40.
[21] Randolph GR, Hagler DJ, Khandheria BK, et al. Remote telemedical interpretation of neonatal echocardiograms: impact on clinical management in a primary care setting. J Am Coll Cardiol 1999;34:241–5.
[22] Paing WW, Weller RA, Welsh B, Foster T, Birnkrant JM, Weller EB. Telemedicine in children and adolescents. Curr Psychiatry Rep 2009;11:114–9.
[23] Diamond JM, Bloch RM. Telepsychiatry assessments of child or adolescent behavior disorders: a review of evidence and issues. Telemed J E Health 2010;16:712–6.

[24] Lazzeri G, Rossi S, Pammolli A, Pilato V, Pozzi T, Giacchi MV. Underweight and overweight among children and adolescents in Tuscany (Italy). Prevalence and short-term trends. J Prev Med Hyg 2008;49:13–21.
[25] Pinhas-Hamiel O, Zeitler P. The global spread of type 2 diabetes mellitus in children and adolescents. J Pediatr 2005;146:693–700.
[26] Nadeau KJ, Zeitler PS, Bauer TA, et al. Insulin resistance in adolescents with type 2 diabetes is associated with impaired exercise capacity. J Clin Endocrinol Metab October 2009;94:3687–95.
[27] Eagle TF, Gurm R, Goldberg CS, et al. Health status and behavior among middle-school children in a midwest community: what are the underpinnings of childhood obesity? Am Heart J 2010;160:1185–9.
[28] Kannel WB, Kannel C, Paffenbarger Jr RS, Cupples LA. Heart rate and cardiovascular mortality: the Framingham Study. Am Heart J 1987;113:1489–94.
[29] Kwok SY, So HK, Choi KC, et al. Resting heart rate in children and adolescents: association with blood pressure, exercise and obesity. Arch Dis Child 2013;98:287–91.
[30] Wändell PE, Carlsson AC, Theobald H. The association between BMI value and long-term mortality. Int J Obes 2009;33:577–82.
[31] Rennie KL, Livingstone MBE, Wells JCK, et al. Association of physical activity with body-composition indexes in children aged 6–8 y at varied risk of obesity. Am J Clin Nutr 2005;82:13–20.
[32] Török K, Szelényi Z, Pórszász J, Molnár D. Low physical performance in obese adolescent boys with metabolic syndrome. Int J Obes Relat Metab Disord 2001;25:966–70.
[33] Gondoni LA, Titon AM, Nibbio F, Augello G, Caetani G, Liuzzi A. Heart rate behavior during an exercise stress test in obese patients. Nutr Metab Cardiovasc Dis 2009;19:170–6.
[34] Gutin B, Islam S, Treiber F, Smith C, Manos T. Fasting insulin concentration is related to cardiovascular reactivity to exercise in children. Pediatrics 1995;96:1123–5.
[35] Laguna M, Aznar S, Lara MT, Lucía A, Ruiz JR. Heart rate recovery is associated with obesity traits and related cardiometabolic risk factors in children and adolescents. Nutr Metab Cardiovasc Dis Dec 1 2012, http://dx.doi.org/10.1016/j.numecd.2012.10.002.
[36] Lin LY, Kuo HK, Lai LP, Lin JL, Tseng CD, Hwang JJ. Inverse correlation between heart rate recovery and metabolic risks in healthy children and adolescents: insight from the National Health and Nutrition Examination Survey 1999–2002. Diabetes Care 2008;31:1015–20.
[37] Cheng YJ, Macera CA, Church TS, Blair SN. Heart rate reserve as a predictor of cardiovascular and all-cause mortality in men. Med Sci Sports Exerc 2002;34:1873–8.
[38] Wändell PE, Carlsson AC, Theobald H. Effect of heart-rate recovery on long-term mortality among men and women. Int J Cardiol 2010;144:276–9.
[39] Cheng YJ, Lauer MS, Earnest CP, et al. Heart rate recovery following maximal exercise testing as a predictor of cardiovascular disease and all-cause mortality in men with diabetes. Diabetes Care 2003;26:2052–7.
[40] Deniz F, Katircibasi MT, Pamukcu B, Binici S, Sanisoglu SY. Association of metabolic syndrome with impaired heart rate recovery and low exercise capacity in young male adults. Clin Endocrinol 2007;66:218–23.
[41] Brinkworth GD, Noakes M, Buckley JD, Clifton PM. Weight loss improves heart rate recovery in overweight and obese men with features of the metabolic syndrome. Am Heart J 2006;152:693.e1–6.
[42] Owens S, Gutin B, Allison J, et al. Effect of physical training on total and visceral fat in obese children. Med Sci Sports Exerc 1999;31:143–8.
[43] Bell LM, Watts K, Siafarikas A, et al. Exercise alone reduces insulin resistance in obese children independently of changes in body composition. J Clin Endocrinol Metab 2007;92:4230–5.
[44] Brunetti ND, Amoruso D, De Gennaro L, et al. Tele-medicine for cardiovascular emergencies: ready for the prime time? J Clin Exp Cardiolog 2012;3:8.

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Intravenous administration of Gr-1+CD11b+ myeloid cells increases neovascularization and improves cardiac function after heart infarction

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The relative importance of bone marrow-derived cell populations to adult neovascularization is not clear. There are increasing evidences that myeloid cell lineage may play a role in neovascularization [1–4]. In a previous report, we demonstrated that Gr-1+CD11b+ myeloid cells improve both angiogenesis and vasculogenesis in tumor [1]. A recent report by Kim et al. showed that muscle-derived Gr1(dim)CD11b(+) myeloid cells enhance neovascularization in an ischemic hind limb model [3]. Similarly, a study with the same ischemic hindlimb model also verified the enhanced neovascularization properties uniquely associated with proangiogenic cells derived from common myeloid progenitors [4]. In the present study, we further investigated whether intravenous administration of Gr1+CD11b+ myeloid cells increases neovascularization and improves cardiac function after heart infarction.

C57BL/6 mice were purchased from Jackson Lab. All animals received humane care and the study protocols were approved by the Vanderbilt Medical University Animal Care and Use Committee.

We sorted Gr-1+CD11b+ myeloid cells from the spleens of mice as previously described [5]. To investigate whether Gr-1+CD11b+ myeloid cells increase angiogenesis *in vitro*, we cultured Gr-1+CD11b+ myeloid cells with aortic ring [6]. At the seventh day, we found that endothelial sprouts in Gr-1+CD11b+ myeloid cell treated group are significantly more than that in no cell treated group (23.2 ± 3.7 *versus* 13.4 ± 2.4 control, $p < 0.01$, $n = 5$ in each group, Fig. 1A and B), which indicated that Gr-1+CD11b+ myeloid cells increase angiogenesis *in vitro*. In order to see whether Gr-1+CD11b+ myeloid cells increase angiogenesis *in vivo*, we performed dorsal window model in mice [7]. We injected Gr-1+CD11b+ myeloid cells into tail vain of mice to see whether injected Gr-1+CD11b+ myeloid cells home to the site of window chamber. By tracing Gr-1+CD11b+ myeloid cells marked with PKH-26 (Fig. 1C-a), we found that the Gr-1+CD11b+ myeloid cells home to the site of the window chamber after intravenous injection (Fig. 1C-b). We further found the intravenous injection of Gr-1+CD11b+ myeloid cells that obviously increase blood vessel branches

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