Comparison of 2-year mortality according to obesity in stabilized patients with type 2 diabetes mellitus after acute myocardial infarction

: results from the DIAMOND (DIabetic Acute Myocardial InfarctiON Disease) prospective cohort registry

Ki-Bum Won[1], Seung-Ho Hur[1], Yun-Kyeong Cho[1], Hyuck-Jun Yoon[1], Chang-Wook Nam[1], Kwon-Bae Kim[1], Jang-Ho Bae[2], Dong-Ju Choi[3], Young-Keun Ahn[4], Jong-Seon Park[5], Hyo-Soo Kim[6], Rak-Kyeong Choi[7], Donghoon Choi[8], Joon-Hong Kim[9], Kyoo-Rok Han[10], Hun-Sik Park[11], So-Yeon Choi[12], Jung-Han Yoon[13], Hyeon-Cheol Kwon[14], Seung-Un Rha[15], Kyung-Kuk Hwang[16], Do-Sun Lim[17], Kyung-Tae Jung[18], Seok-Kyu Oh[19], Jae-Hwan Lee[20], Eun-Seok Shin[21], Kee-Sik Kim[22]

[1]Division of Cardiology, Keimyung University Dongsan Medical Center, Daegu, Korea; [2]Division of Cardiology, Konyang University Hospital, Daejeon, Korea; [3]Division of Cardiology, Seoul National University Bundang Hospital, Seongnam, Korea; [4]Division of Cardiology, Chonnam National University Hospital, Gwangju, Korea; [5]Division of Cardiology, Yeungnam University Hospital, Daegu, Korea; [6]Division of Cardiology, Seoul National University Hospital, Seoul, Korea; [7]Division of Cardiology, Sejong General Hospital, Bucheon, Korea; [8]Division of Cardiology, Yonsei University Severance Hospital, Seoul, Korea; [9]Division of Cardiology, Pusan National University Yangsan Hospital, Yangsan, Korea; [10]Division of Cardiology, Hallym University Kangdong Sacred Heart Hospital, Seoul, Korea; [11]Division of Cardiology, Kyungpook National University Hospital, Daegu, Korea; [12]Division of Cardiology, Ajou University Hospital, Suwon, Korea; [13]Division of Cardiology, Wonju Severance Christian Hospital, Wonju, Korea; [14]Division of Cardiology, Samsung Medical Center, Seoul, Korea; [15]Division of Cardiology, Korea University Guro Hospital, Seoul, Korea; [16]Division of Cardiology, Chungbuk National University Hospital, Cheongju, Korea; [17]Division of Cardiology, Korea University Anam Hospital, Seoul, Korea; [18]Division of Cardiology, Eulji University Hospital, Daejeon, Korea; [19]Division of Cardiology, Wonkwang University Hospital, Iksan, Korea; [20]Division of Cardiology, Chungnam National University Hospital, Daejeon, Korea; [21]Division of Cardiology, Ulsan University Hospital, Ulsan, Korea; [22]Division of Cardiology, Daegu Catholic University Medical Center, Daegu, Korea

Presenter:

Ki-Bum Won, Division of Cardiology, Keimyung University Dongsan Medical Center

Background

- Diabetes mellitus (DM) is strongly associated with adverse cardiovascular (CV) event occurrence.

Grundy SM et al. Circulation 1999; 100:1134–1146.

- DM is considered as a coronary artery disease (CAD) risk-equivalent because the risk of acute myocardial infarction (AMI) in DM patients without evidence of CAD matches that of patients without DM with a previous history of AMI.

Haffner SM et al. N Engl J Med 1998; 339: 229–234.

- Obesity is one of the major factors for insulin resistance.

Welsh M et al. Diabetes Metab Rev 1993; 9:25–36.
DeFronzo RA. Med clin North Am 2004; 88:787–835.

- It is well-known that the clinical features of type 2 DM (T2DM) in Asia are explicitly different from those in other parts of the world.

- People in Asia tend to develop DM with a lesser degree of obesity at younger ages, suffer longer with complications of diabetes, and die sooner than people in other regions.

Yoon KH et al. Lancet 2006; 368:1681–1688.

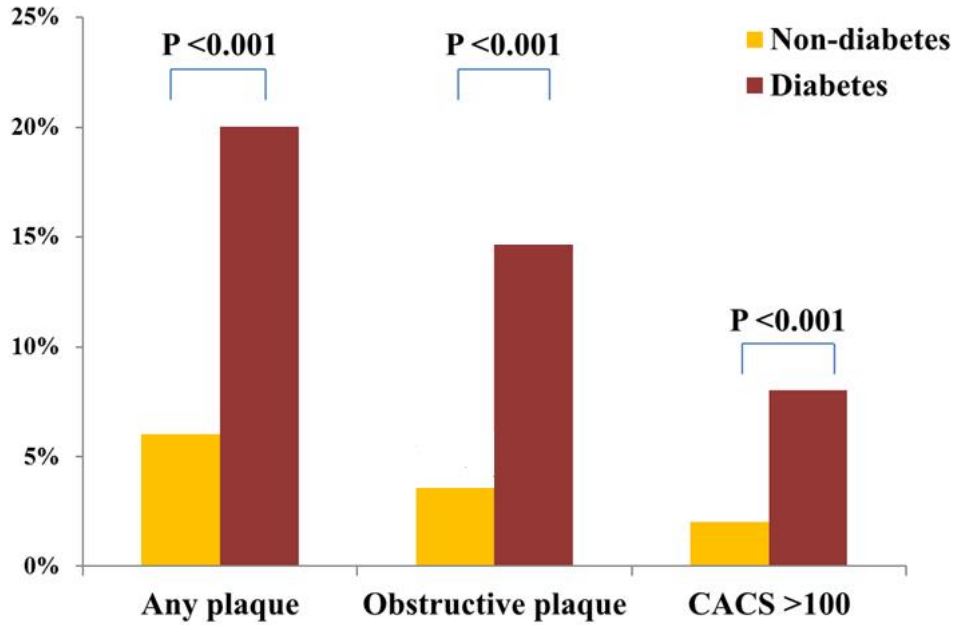
- **In Korea,**
  - The majority of DM patients are not obese, even with obesity defined as a body mass index (BMI) ≥25 kg/m^2.
  - Impaired insulin secretion is more prominent than insulin resistance in T2DM, even in the status of impaired glucose tolerance

Park JY et al. Diabetes Res Clin Pract 1997; 35:49–56.
Shin CS et al. Diabetes Care 1997; 20:1842–1846.
Kim DJ et al. Metabolism 2001; 50:590–593.

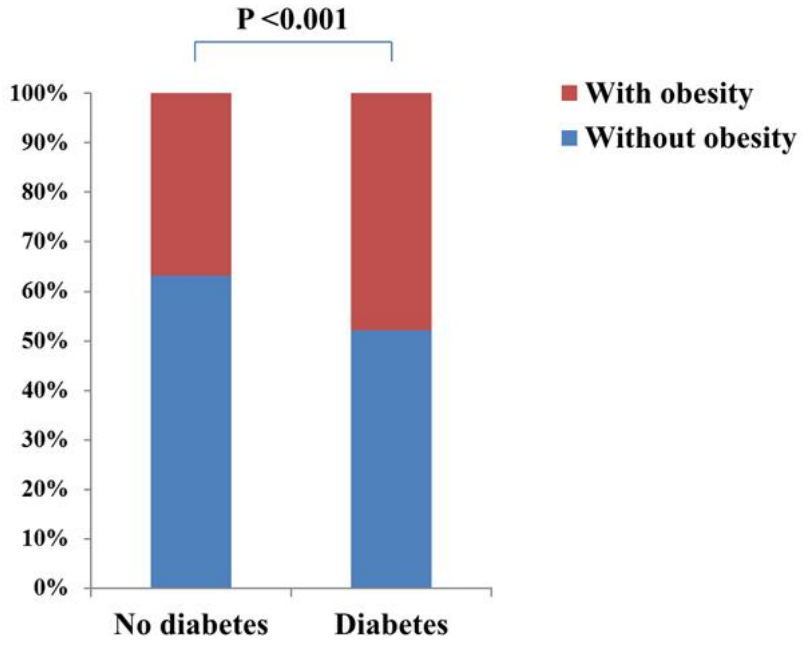
Type 2 DM, obesity, and coronary artery disease in general Korean population

Won et al. Diabetology & Metabolic Syndrome 2014; 6:134

CAD parameters according to DM



Prevalence of obesity according to DM

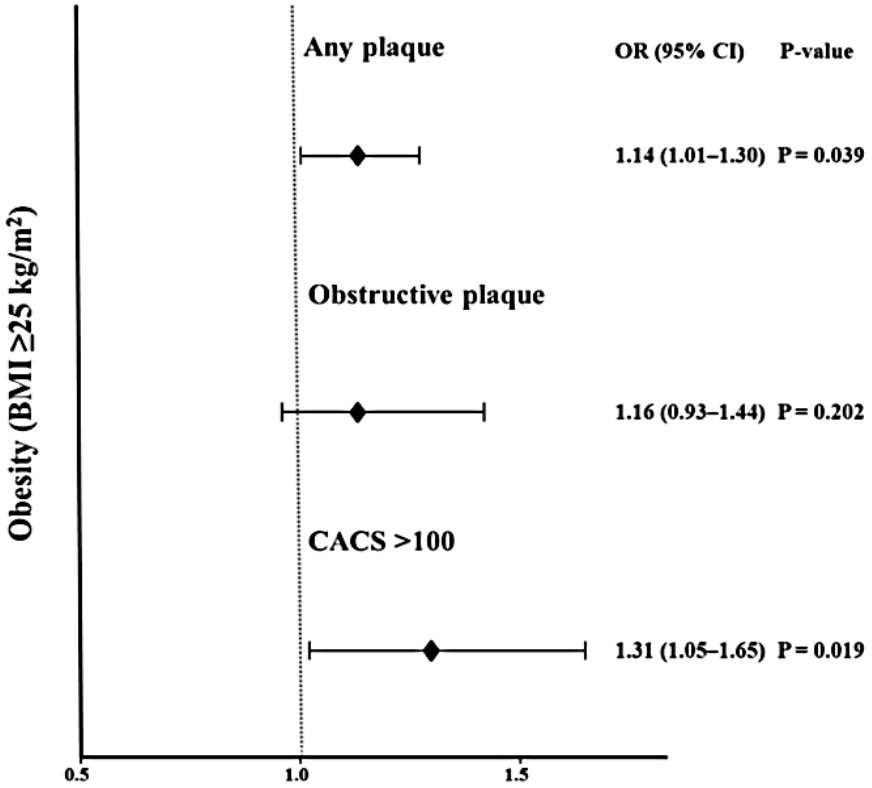


Type 2 DM, obesity, and coronary artery disease in general Korean population

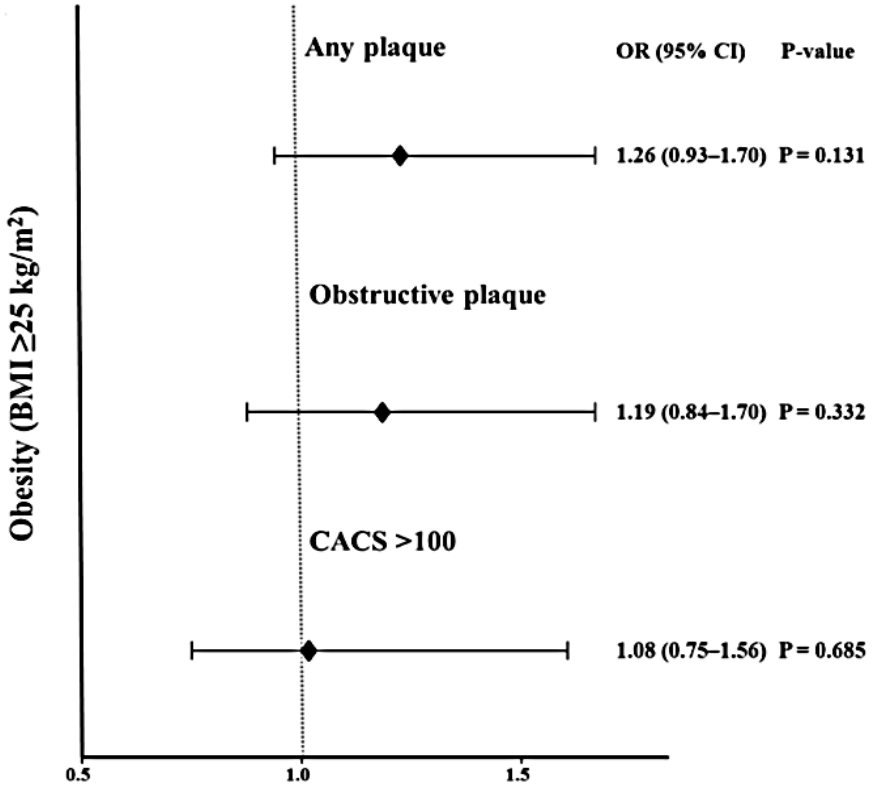
Won et al. Diabetology & Metabolic Syndrome 2014; 6:134

Predictive value of obesity for CAD parameters according to DM

(A) Non-diabetes



(B) Diabetes



Obesity paradox

- In the genral population, obesity increases the risk of numerous comorbidities and CV disease.

Wilson PF et al. Arch Intern Med 2002; 162: 1867–72.

- However, obesity appearing to be associated with improved survival has been replicated after major CV events such as AMI.

Buettner HJ et al. Eur Heart J 2007, 28: 1694–701.
Bucholz EM et al. Am J Med 2012, 125: 796–803.
Won KB et al. Catheter Cardiovasc Interv 2014, 83: 713–720.

- There is a paucity of data on the association between obesity and mortality in diabetic patients after the event of AMI.
  - Identifying this issue may be more important in the Asian T2DM population considering the explicitly different features of T2DM in Asia.

- Furthermore, it is necessary to evaluate this association in stabilized patients after AMI because it is difficult to identify the individual impact of clinical factors on early-term events after AMI.

Objective

- To evaluate the association between obesity and 2-year mortality in stabilized T2DM patients after AMI in the Korean population using the data of DIAMOND registry.

Methods

- **DIAMOND registry**
  - Prospective, multicenter, observational study
  - Between April 2010 and June 2012
  - 22 university or tertiary hospitals participated in this study
  - All participants were T2DM patients after the event of AMI

- **Stabilized AMI patients:** Subjects who did not have any clinical events within one month after the initial presentation of AMI.

- **Obesity:** A BMI of ≥25 kg/m^2.

❖ Inclusion criteria

- T2DM patients with age ≥45 years
- Documented STEMI or NSTEMI

  : CK-MB >3 times upper limit of normal and troponin-I >upper normal limit

  : Angiographically ≥50% luminal stenosis) with intracoronary filling defect or haziness suggesting coronary thrombus/vulnerable plaque

  : Coronary spasm induced AMI defined by an elevated cardiac enzymes without significant stenosis

❖ Exclusion criteria

- Any adverse clinical event within one month after the initial presentation of AMI

- Among a total of 1,192 consecutive T2DM subjects with AMI, 1,125 stabilized T2DM patients were finally enrolled.

- **Clinical endpoints:**
  - Cardiac death and all-cause death during 2-year follow-up.
  - All death was considered cardiac unless there was a clear non-cardiac cause.

- **Follow-up protocol:** all patients were contacted at 1, 6, 12, and 24 months after the index procedures.

Results – Patients characteristics

	Obese T2DM (n = 427)	Non-obese T2DM (n = 698)	P
Age, years	63 ± 10	66 ± 10	<0.001
Male	283 (66)	457 (66)	0.783
BMI, kg/m^2	27.1 ± 2.0	22.3 ± 1.8	<0.001
Co-existing conditions, n (%)			
Hypertension	294 (69)	448 (64)	0.109
Dyslipidemia	134 (31)	169 (24)	0.009
Previous MI	22 (5)	39 (6)	0.754
Smoking, n (%)	143 (34)	229 (33)	0.814
STEMI, n (%)	204 (48)	326 (47)	0.727
DM duration, years	9.8 ± 8.2	11.5 ± 8.5	0.003
LVEF	53 ± 11	50 ± 12	<0.001
eGFR, mL/min/1.73m^2	76 ± 29	72 ± 33	0.105

Results – Laboratory findings

	Obese T2DM (n = 427)	Non-obese T2DM (n = 698)	P
Laboratory			
Total cholesterol, mg/dL	178 ± 46	170 ± 46	0.004
Triglyceride, mg/dL	146 ± 98	131 ± 100	0.022
LDL, mg/dL	109 ± 40	101 ± 41	0.002
HDL, mg/dL	44 ± 28	44 ± 17	0.988
Creatinine, mg/dL	1.2 ± 1.3	1.3 ± 1.4	0.130
HbA1c, %	7.8 ± 1.4	7.9 ± 1.6	0.370
hs-CRP, mg/dL	4.6 ± 15.9	6.9 ± 23.9	0.081
NT-ProBNP, pg/mL	2,836 ± 7,592	4,040 ± 9,074	0.096
Peak CK-MB, ng/mL	82 ± 114	83 ± 137	0.880
Troponin-I, ng/mL	29 ± 62	31 ± 59	0.637

Results – Medical treatment

	Obese T2DM (n = 427)	Non-obese T2DM (n = 698)	P
Medication at discharge, n (%)			
Aspirin	423 (99)	683 (98)	0.126
Clopidogrel	409 (96)	661 (95)	0.413
Cilostazol	83 (19)	131 (19)	0.781
Beta blocker	364 (85)	591 (85)	0.794
ACEI / ARB	355 (83)	586 (84)	0.720
Statin	365 (86)	572 (82)	0.123
Nitrate	111 (26)	205 (29)	0.222
Nicorandil	77 (18)	149 (21)	0.178
Insulin	51 (12)	119 (17)	0.020

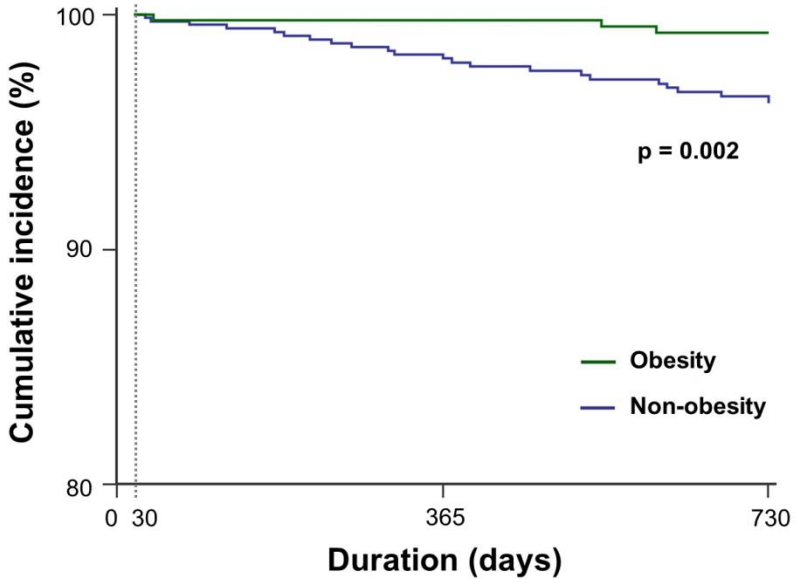
Results – Angiographic & procedural findings

	Obese T2DM (n = 427)	Non-obese T2DM (n = 698)	P
Target vessel of LAD, n (%)	209 (49)	355 (51)	0.533
Target vessel of LM, n (%)	11 (3)	17 (2)	0.883
Multivessel disease, n (%)	254 (60)	414 (59)	0.954
Type B2/C lesion, n (%)	340 (82)	543 (83)	0.850
Pre-PCI TIMI 0, n (%)	173 (42)	260 (40)	0.465
Post-PCI TIMI 2/3, n (%)	400 (97)	639 (97)	0.592
Use of DES, n (%)	341 (93)	540 (93)	0.684
Stent diameter, mm	3.18 ± 0.46	3.07 ± 0.43	<0.001
Stent length, mm	25.4 ± 9.6	24.8 ± 7.9	0.324
Number of implanted stents	1.6 ± 0.9	1.5 ± 0.8	0.703

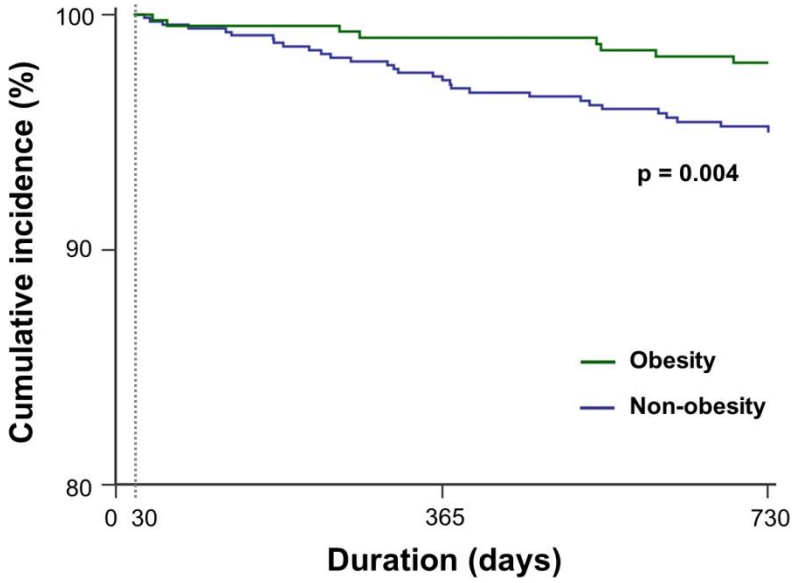
Results – Clinical outcomes

	Obese T2DM (n = 427)	Non-obese T2DM (n = 698)	P
2-year clinical outcomes, n (%)			
Cardiac death	3 (0.7)	25 (3.6)	0.003
All-cause death	8 (1.9)	36 (5.2)	0.006

(A) Cardiac death



(B) All-cause death



Results – Independent determinants

	Cardiac death			
	Univariate		Multivariate	
	HR (95% CI)	P	HR (95% CI)	P
Age ≥65 years	4.52 (1.72–11.88)	0.002	2.65 (0.98–7.15)	0.055
Male	0.68 (0.32–1.44)	0.317		
Previous MI	3.07 (1.07–8.85)	0.038	2.37 (0.81–6.94)	0.114
Hypertension	1.94 (0.79–4.79)	0.150		
Dyslipidemia	1.33 (0.60–2.94)	0.481		
Chronic kidney disease	3.62 (1.70–7.73)	0.001	2.47 (1.11–5.54)	0.028
Multivessel disease	1.19 (0.55–2.57)	0.663		
HbA1c, %	1.17 (0.90–1.52)	0.245		
Stent diameter ≤2.75 mm	0.87 (0.28–2.75)	0.817		
Stent length ≥28 mm	1.62 (0.59–4.49)	0.350		
LVEF <35%	6.09 (2.79–13.30)	<0.001	4.18 (1.90–9.23)	<0.001
Obesity	0.18 (0.06–0.60)	0.005	0.24 (0.07–0.78)	0.018

Results – Independent determinants

	All-cause death			
	Univariate		Multivariate	
	HR (95% CI)	P	HR (95% CI)	P
Age ≥65 years	3.99 (1.91–8.31)	<0.001	2.58 (1.09–6.10)	0.031
Male	0.56 (0.31–1.02)	0.056	0.63 (0.34–1.19)	0.157
Previous MI	2.41 (0.95–6.11)	0.065	1.80 (0.70–4.63)	0.227
Hypertension	1.98 (0.95–4.13)	0.069	1.35 (0.60–3.00)	0.466
Dyslipidemia	1.21 (0.63–2.32)	0.563		
Chronic kidney disease	4.38 (2.34–8.21)	<0.001	3.10 (1.56–6.17)	0.001
Multivessel disease	1.08 (0.59–1.99)	0.801		
HbA1c, %	1.01 (0.80–1.29)	0.920		
Stent diameter ≤2.75 mm	0.71 (0.29–1.76)	0.456		
Stent length ≥28 mm	1.86 (0.88–3.95)	0.105		
LVEF <35%	4.77 (2.47–9.21)	<0.001	3.35 (1.72–6.53)	<0.001
Obesity	0.34 (0.16–0.73)	0.005	0.44 (0.20–0.95)	0.038

Summary

1) The majority (62%) of Korean T2DM patients with AMI are non-obese.
- The incidence of BMI <18.5 kg/m^2 and BMI ≥30 kg/m^2 was only 2.2% and 3.6% in the present study.

2) The incidence of CKD and insulin use were significantly higher in non-obese T2DM patients with AMI.

3) Obese T2DM patients had higher incidence of dyslipidemia and higher LV systolic function after AMI.

Summary

4) Two-year cardiac and all-cause mortality was significantly lower in T2DM patients with than without obesity (cardiac death: 0.7 vs. 3.6%; all-cause death: 1.9 vs. 5.2%) (P <0.05, respectively).

5) The cumulative incidence of cardiac and all-cause death was significantly lower in T2DM patients with obesity than in those without obesity.

6) Obesity was independently associated with decreased cardiac and all-cause mortality after adjusting for confounding clinical factors.

Limitations

- Difficulty to identify the range of BMI for the beneficial effect of obesity in T2DM patients after AMI because only 3.6% of our diabetic patients had a BMI ≥30 kg/m^2.

  - It might be related to the typical characteristics of DM in Asia.

- Only used BMI to define obesity

  - It might not be the ideal measure to discriminate between fat and lean body mass to identify obesity status.

  - However, previous studies reported that BMI was significantly associated with abdominal fat and waist circumference in Korean subjects.

Conclusions

- In a Korean population of stabilized diabetic patients after AMI, non-obese patients appear to have higher cardiac and all-cause mortality compared with obese patients after adjusting for confounding factors.

Published in Cardiovascular Diabetology 2015; 14: 141.

Thank you for your attention!!