# Haptoglobin Genotype as a Prognostic Factor for Operation-Related Morbidity in Coronary Artery Bypass Grafting Patients

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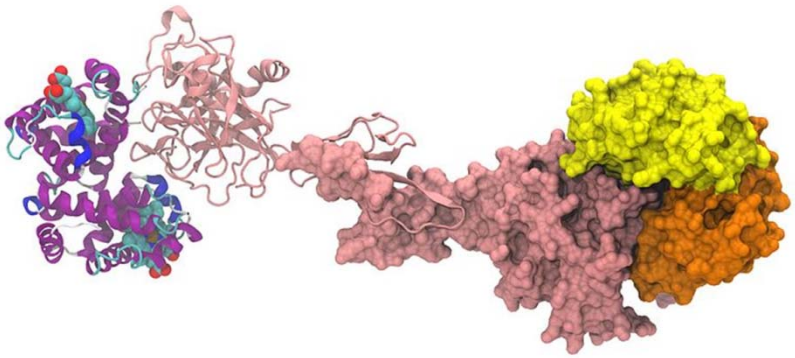
# Disclosure

- None

# Haptoglobin (Hp)

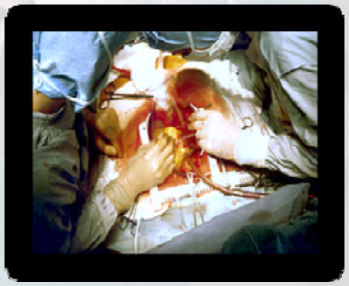
- Haptoglobin binds free plasma hemoglobin; a **decrease** in haptoglobin can support a diagnosis of **hemolytic anemia.**
- Haptoglobin has two allelic forms - Hp1 and Hp2. Three genotypes are found in humans: Hp1-1 (16%), Hp2-1 (48%), and Hp2-2 (36%).
- Hp of different genotypes have been shown to bind hemoglobin with different affinities, **with Hp2-2 being the weakest binder.**



# Haptoglobin, CVD and Diabetes

- Type 1 diabetes patients who carry the **Hp1-1 phenotype are at lower risk of developing retinopathy and nephropathy.**
- Diabetic patients with the Hp **2-1 phenotype are more likely to have collaterals** than diabetic patients with the Hp 2-2 phenotype.
- Individuals with **type 2 diabetes** and the **Hp2-2 phenotype** have a **2-5-fold greater risk of developing CVD** when compared to individuals with the Hp1-1 phenotype.
- Hp 2-2 phenotype in diabetic patients is a independent predictor of Major Adverse Cardiovascular Events **(MACE) and restenosis in the 1-year period after PTCA.**

# Study rationale



Complexity

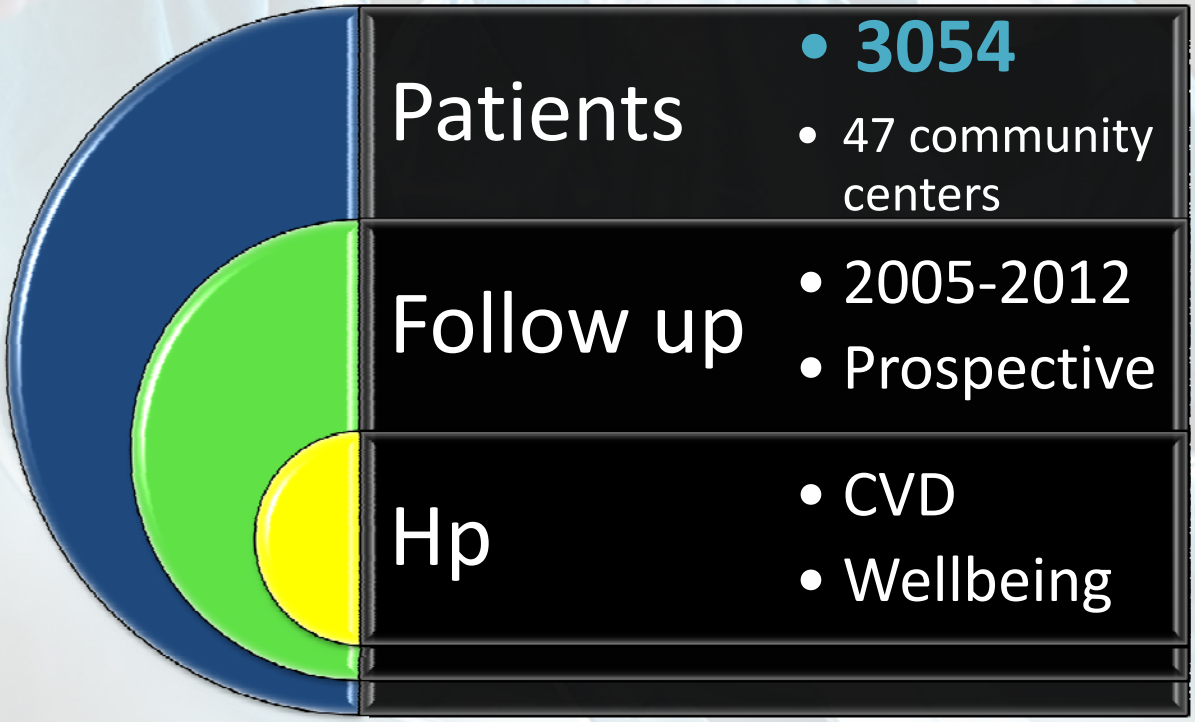
M&M

Rehabilitation

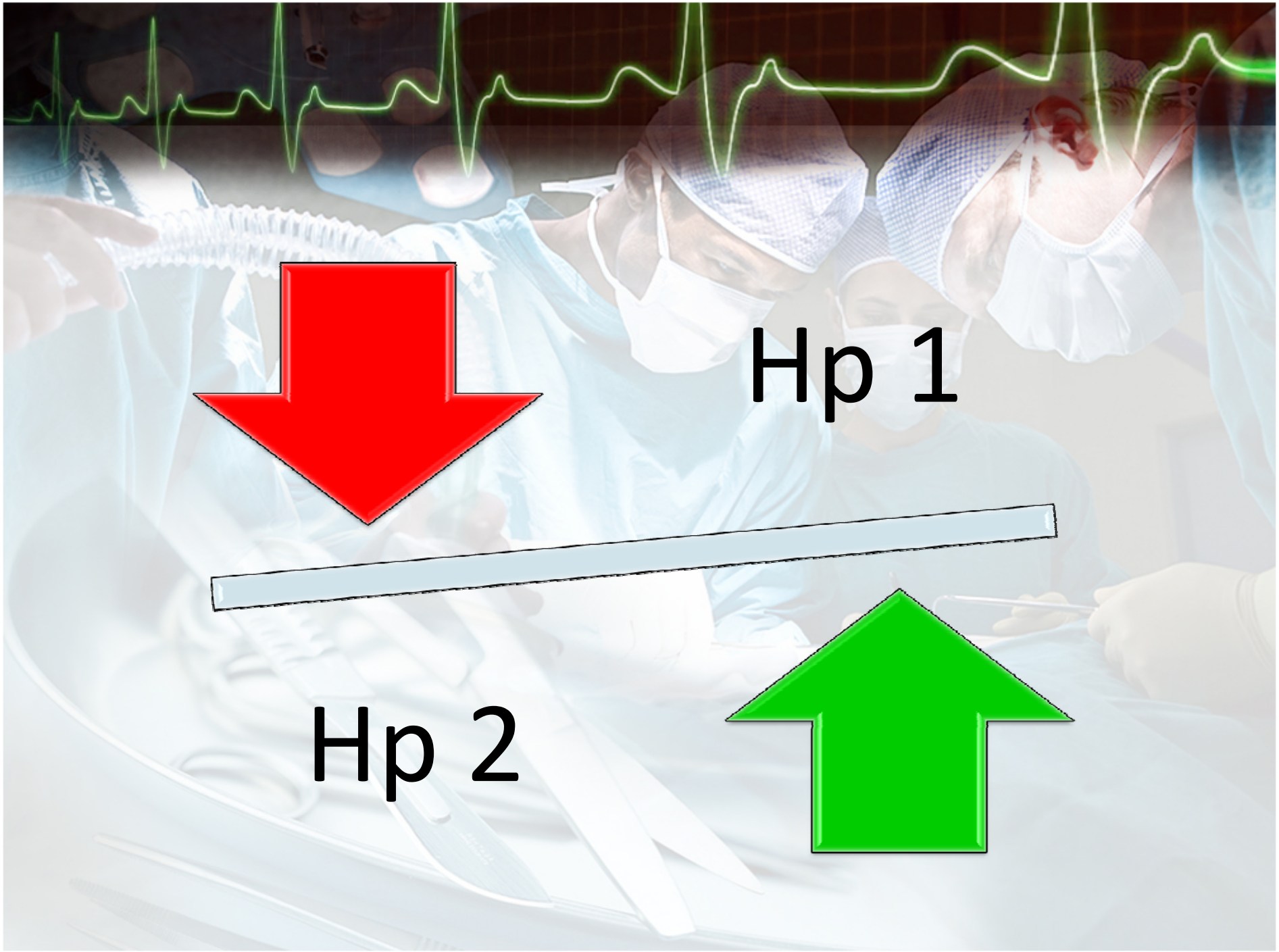
CABG

Hp

# Research synopsis



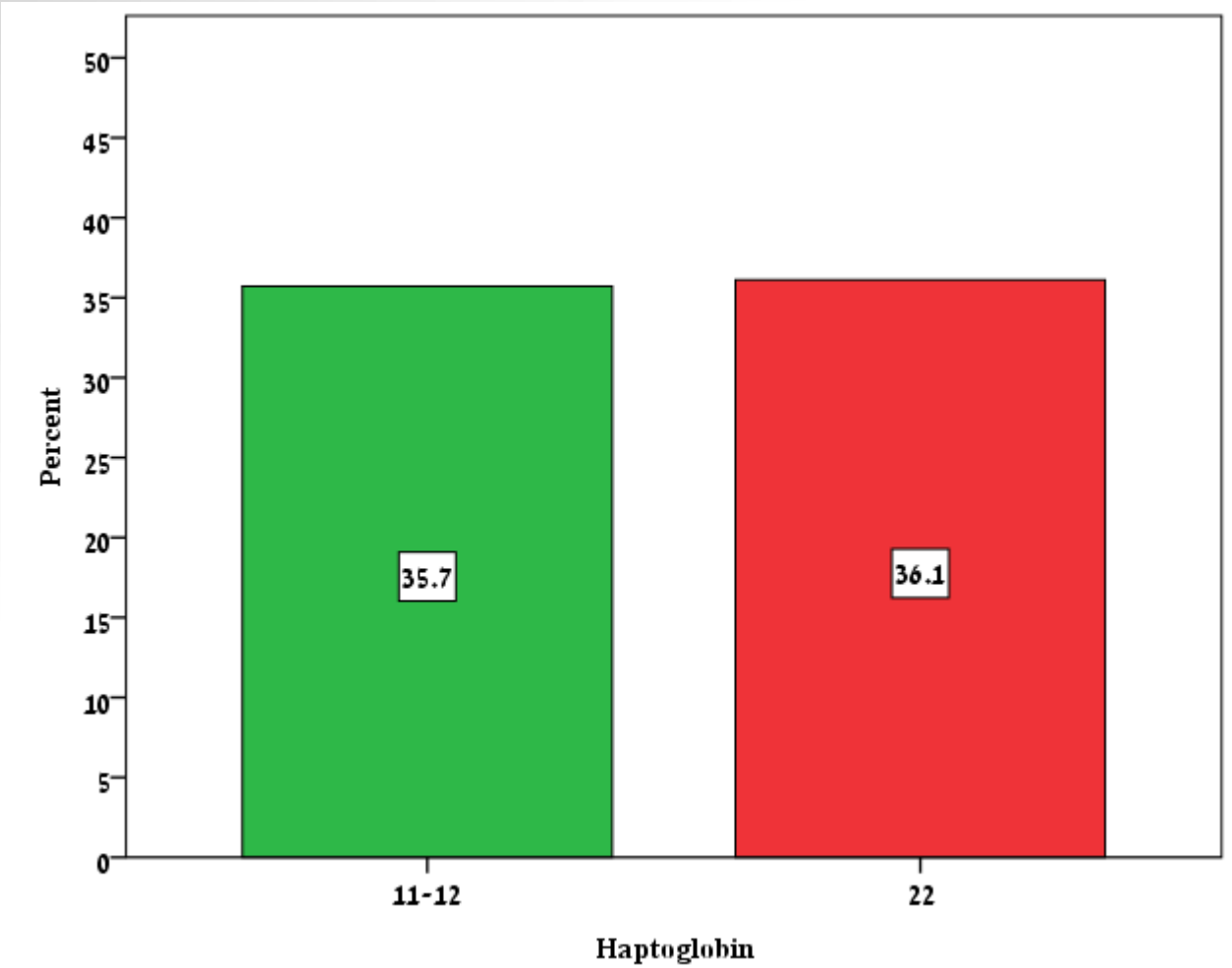

**Genomic medicine**


Hp 1
Hp 2

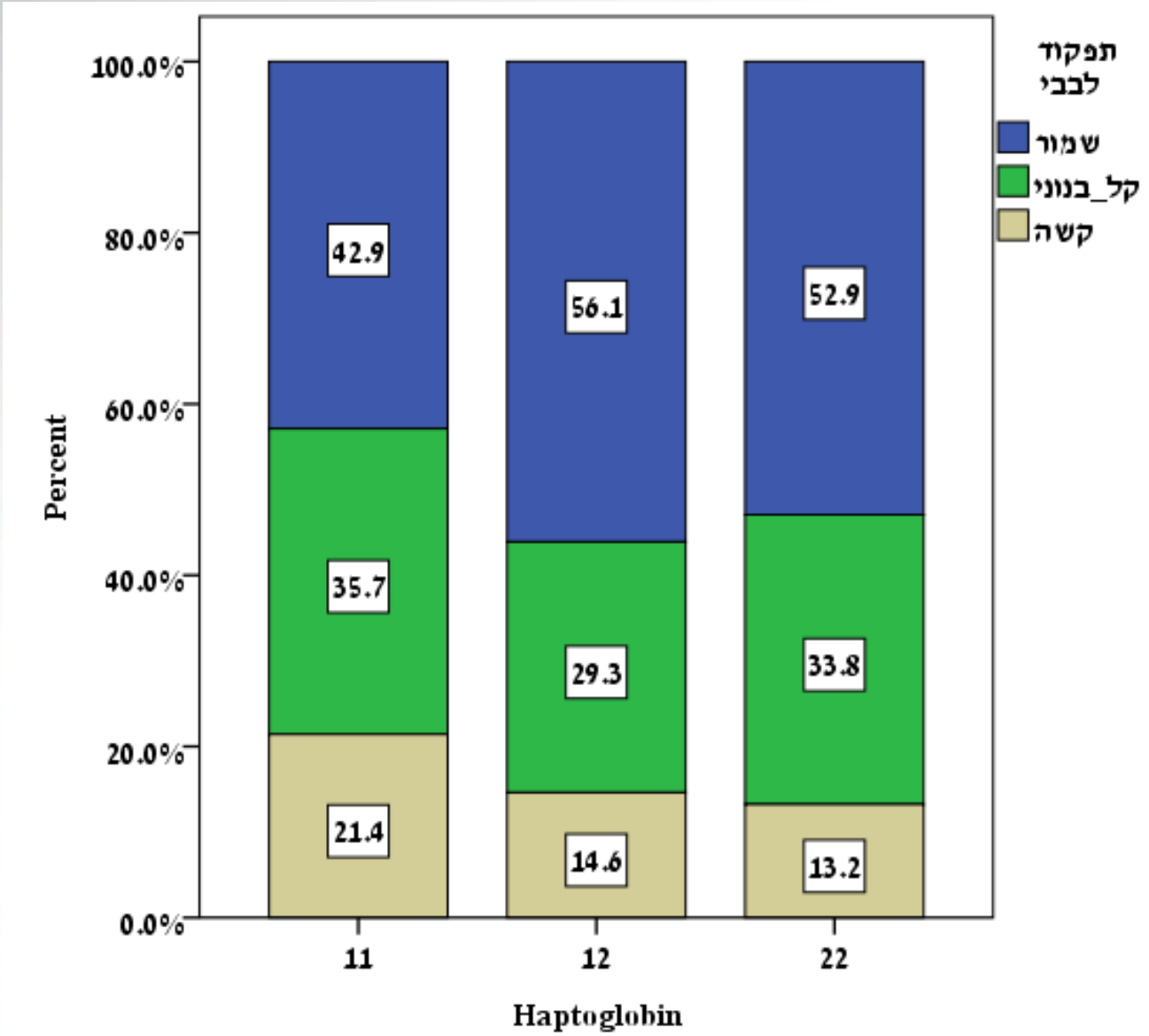
# CABG - Demographics

| Haptoglobin<br>N | 11<br>285 | 12<br>1248 | 22<br>1511 | |
|---|---|---|---|---|
| N(%) | 13(10.3) | 42(33.3) | 71(56.3) | |
| | mean ± std | | | P value |
| Age | 68.7 ± 5.6 | 69.3 ± 9.2 | 67.9 ± 9.4 | 0.74 |
| Duration of DM | 9.6 ± 5.12 | 10.3 ± 7.5 | 12.8 ± 8.8 | 0.18 |
| BMI | 28.6 ± 5.8 | 28.4 ± 6.0 | 28.7 ± 4.2 | 0.90 |
| | % | | | |
| Males | 76.9 | 83.3 | 66.2 | 0.13 |
| Minorities | 7.7 | 16.7 | 5.7 | 0.17 |
| Current smoker | - | 4.8 | 7.0 | 0.10 |
| Hypertension | 92.3 | 81.0 | 70.4 | 0.18 |
| IHD | 84.6 | 64.3 | 63.4 | 0.35 |
| MI | 30.8 | 38.1 | 35.2 | 0.89 |
| CVA | 7.7 | 9.5 | 5.6 | 0.59 |
| TIA | 7.7 | 14.3 | 7.0 | 0.49 |
| Coronary Cath. | 76.9 | 54.8 | 52.1 | 0.28 |
| PCI | 30.8 | 33.3 | 25.4 | 0.65 |
| CEA | 7.7 | 7.1 | 4.2 | 0.60 |

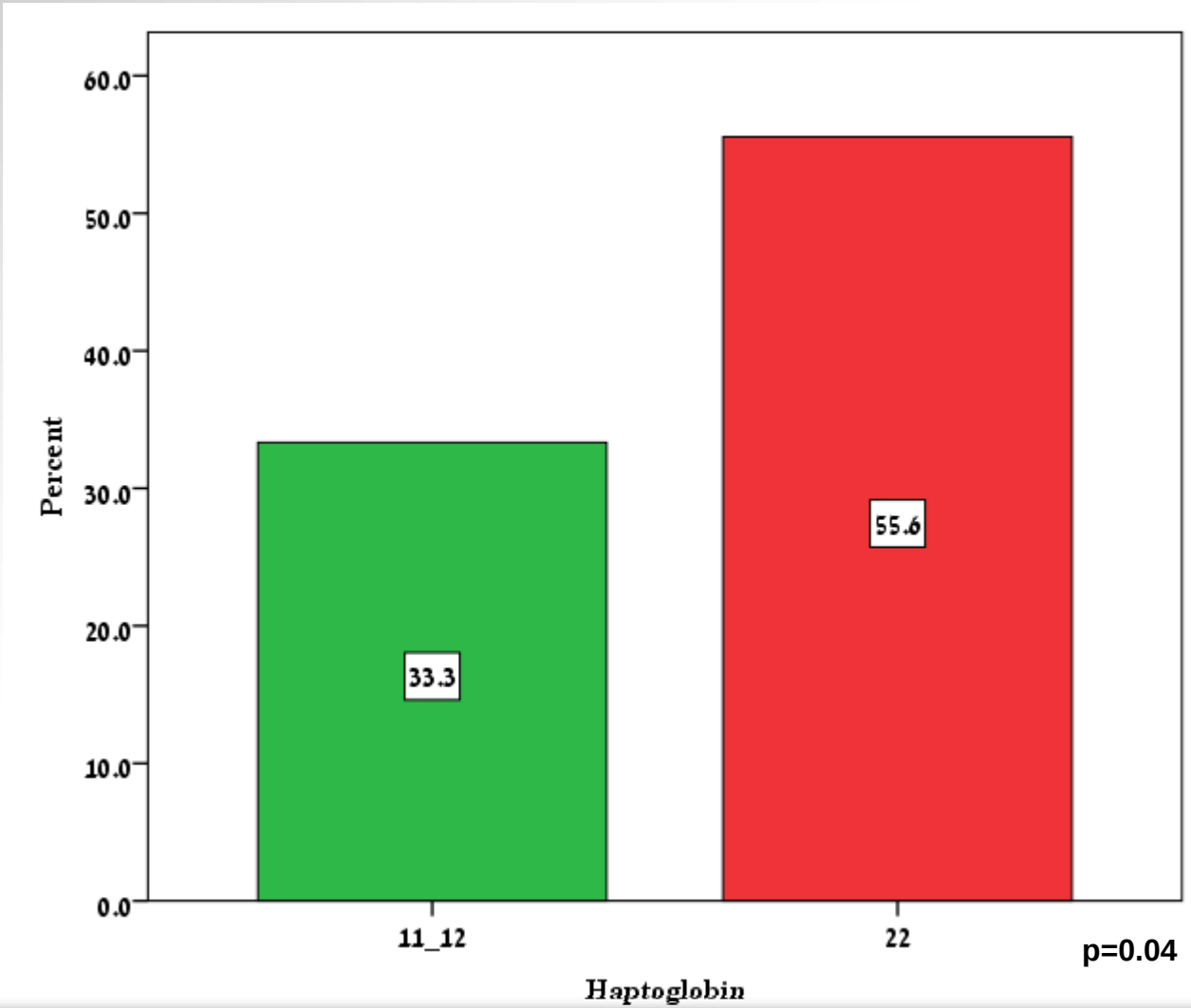
# Prior Myocardial Infraction



# Cardiac function

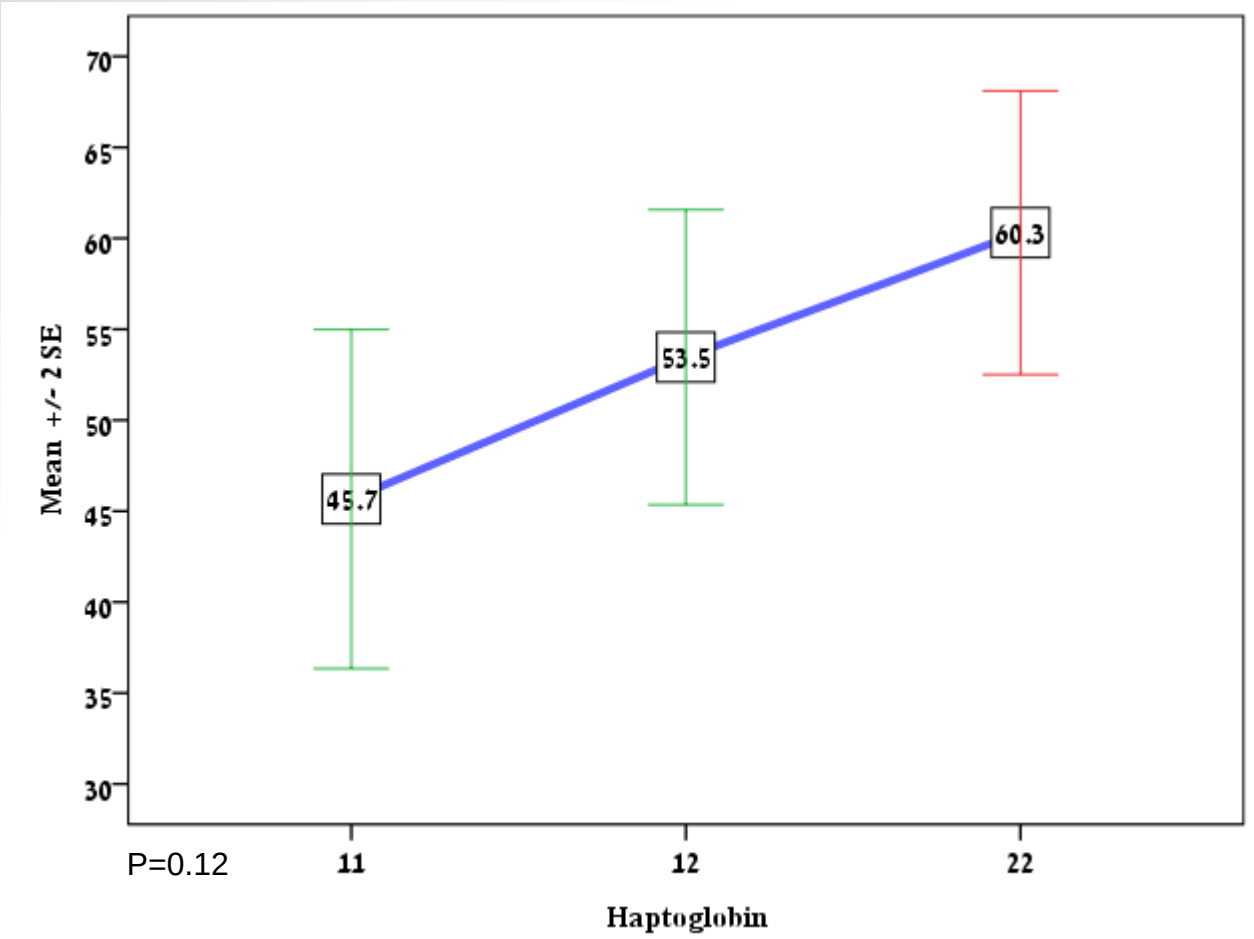


# Hp 2-2 bypass time is longer

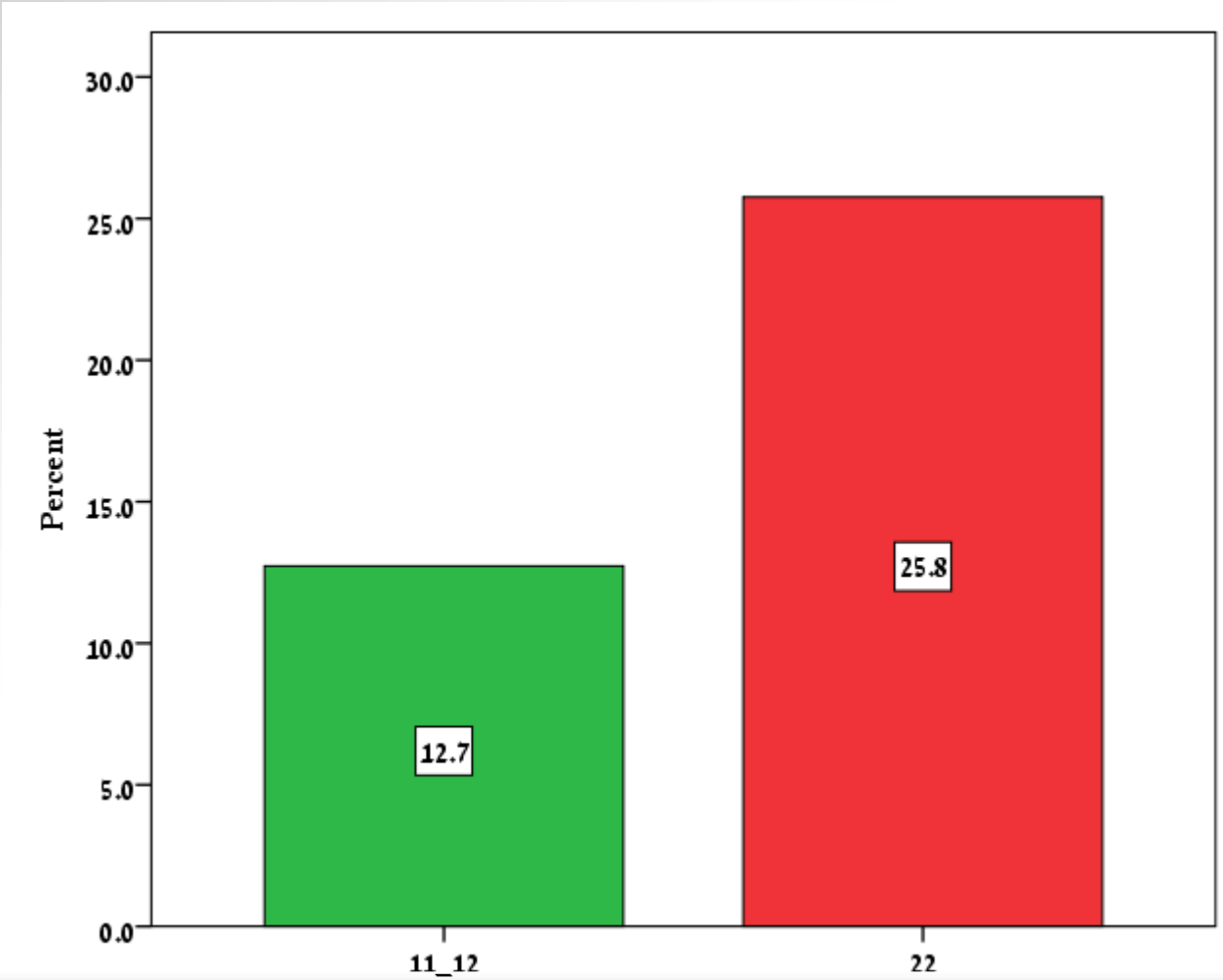



On Bypass > 80 Minutes (median)

# Aortic cross-clamp length

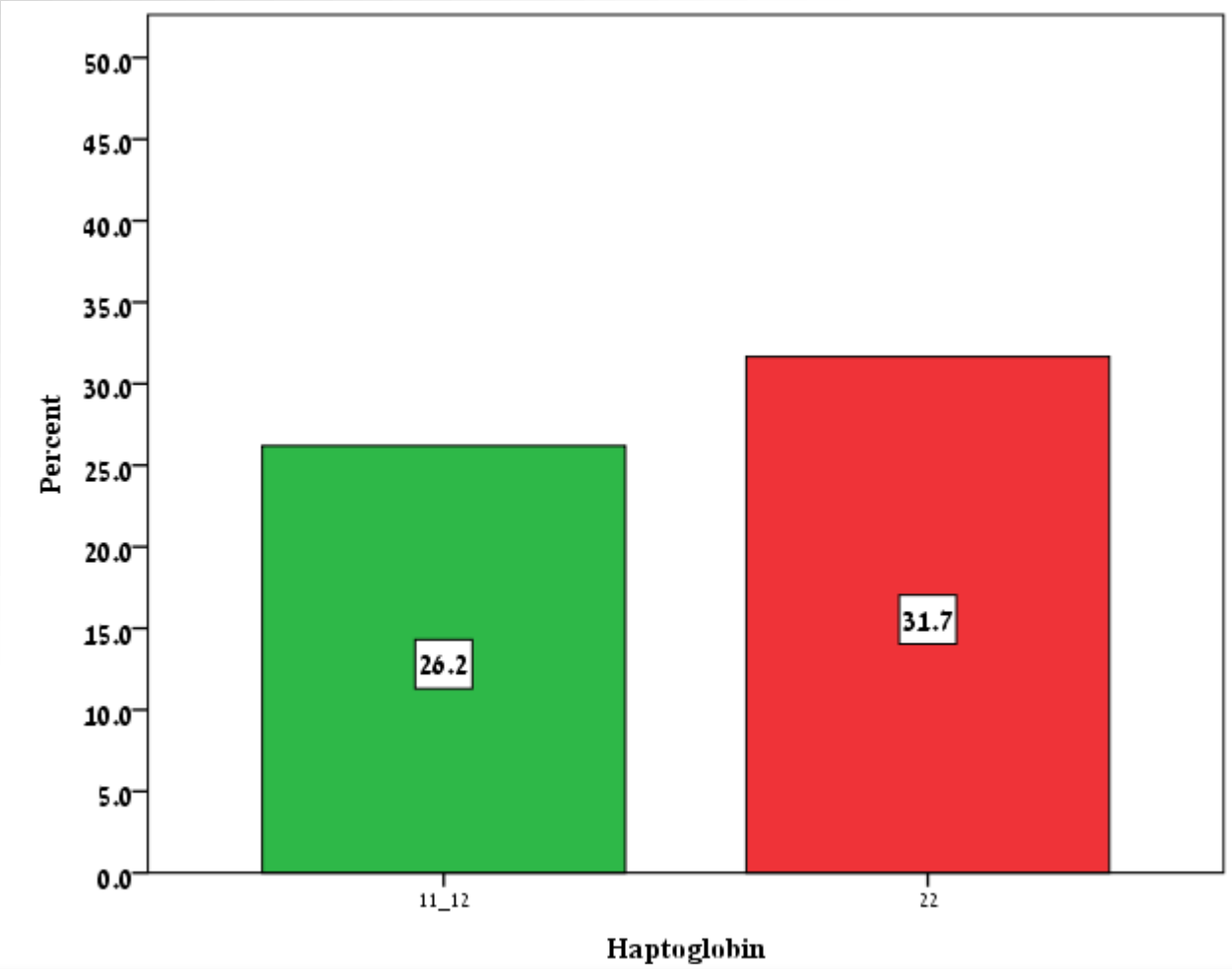


# Hp 2-2 patients increase trend in arterial revascularization



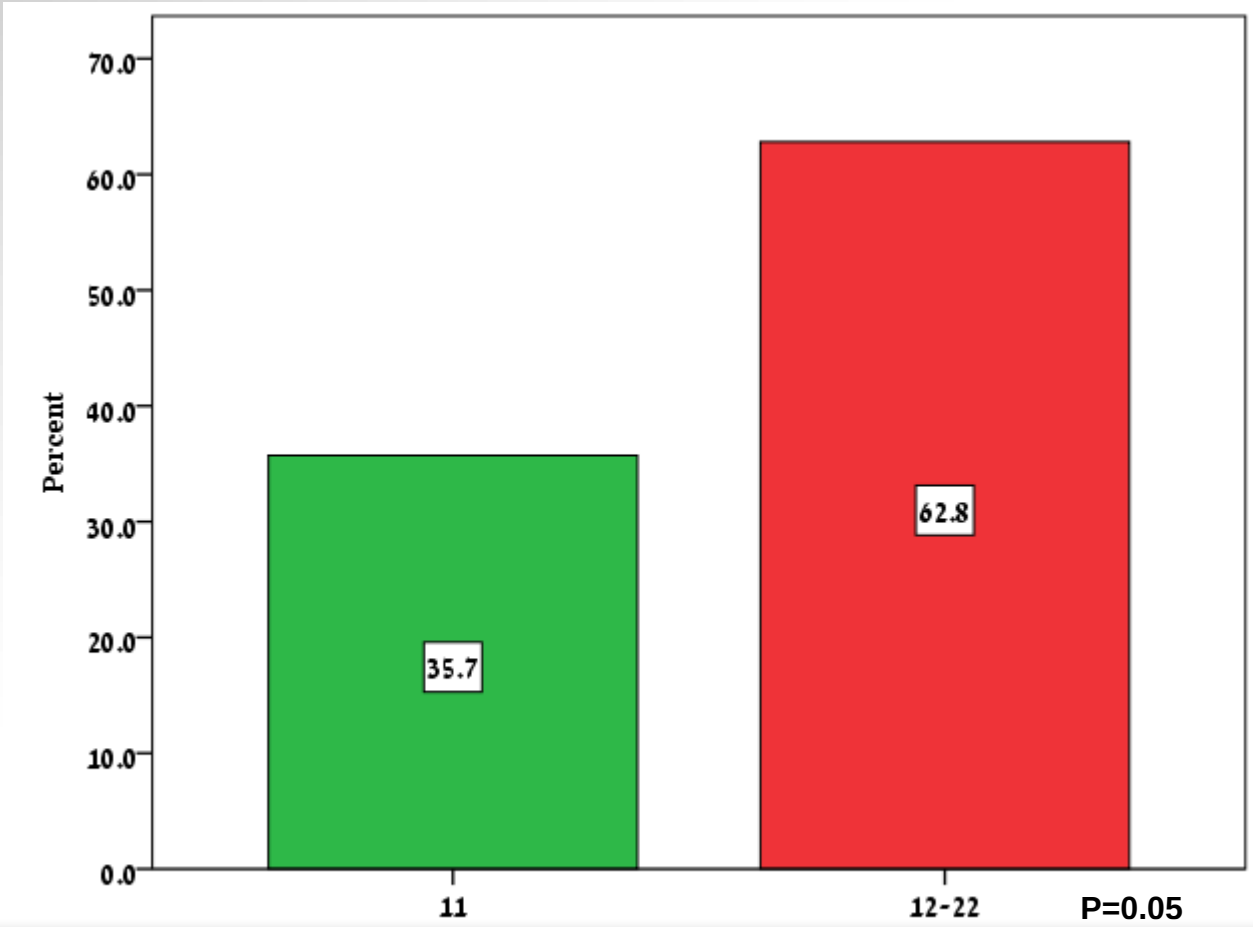

**Double mammary arteries**

# No difference in the total number of bypasses



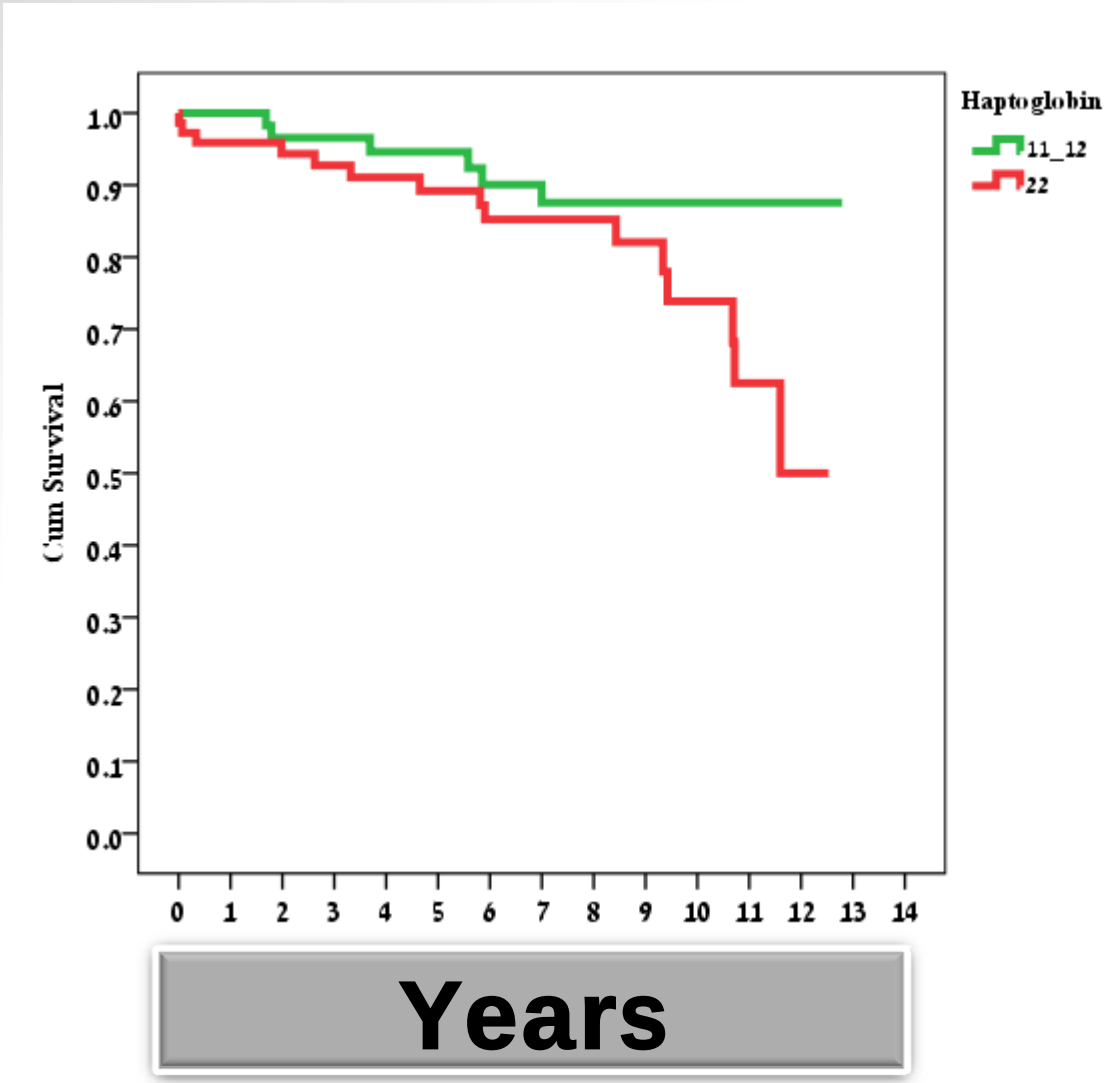

**Number of bypasses > 3**

# Hp 2 patients are hospitalized longer




**Hospitalization duration > 1 week (post procedure)**

# A trend towards survival reduction in Hp 2-2 patients



# Study limitations

- Study population
  - Diabetic patients vs CABG patients
- Patient age > 55

# Conclusion

- Extended postoperative hospitalizations, reflecting complex post-operative recovery, **suggest prognostic potential** in the Hp 2 allele regarding possible post-CABG surgery complications.

- Post surgery recovery is worse even for Hp 2-1 patients.

# Future Genomic medicine

- Hp 2 should be considered as a possible risk factor for post CABG morbidity
- Early follow up and diagnosis
- Earlier CABG
- Hospital and Community rehabilitation

# THANK YOU!

- Professor Endy Levy lab
- Carmel statistical analysis team
- Clinical Research Unit, Clalit Health Care, Haifa district
- Professor Dan Aravot and Dr. Chen Shapira

# Prior work

- A leading group from Belgium has investigated the relationship between Hp genotype and the extension of coronary lesions in 765 male patients who underwent coronary artery bypass grafting (CABG).
- In this group, relative Hp1 (0.418) and Hp2 (0.582) allele frequencies were comparable with those of the reference population.
- Candidate CABG patients with a Hp 2-2 type were overrepresented in the younger (< 45 years) age group ($p < 0.05$).
- Hp 2-2 patients needed more bypass grafts than Hp 1-1 patients (relative risk 1.92 95% C.I. 1.24-2.96).
- The Hp 2-2 type was overrepresented among victims of a previous acute myocardial infarction ($p < 0.05$) and among younger patients (< 45 years) at infarction ($p < 0.05$).
- In patients who already underwent a previous CABG, graft survival time was shortest in those bearing Hp 2-2 ($p < 0.05$)
- In conclusion, it is evident that the haptoglobin genotype is an independent risk factor for CVD complications especially in the setting of diabetes mellitus.