synthesis in the liver from Acetyl-CoAm, which is regulated by feed back inhibition on reductase hydroxyl -methyl - glutary -CoA (HMGCoA) reductase by excess cholesterol. A high cholesterol diet causes decreased synthesis, and the excess is excreted in bile. The excreted bile salts are very efficiently reabsorbed more than dietary cholesterol.

Significant correlations have been found among the studied parameters in both groups studied, for example, between uric acid and albumin in the post-exercise male control group and in the pre and post-exercise control female group. There was a significant correlation between uric acid and albumin in the pre-exercised male patient group, and post-exercise female patients group. As well as between LDL and MDA in the post-exercise male control group and in the pre-exercise female patients' and VLDL and MDA in the post-exercise male control group. A significant correlation was found to exist between TG and MDA in the post-exercise female control group.

In conclusion, treadmill exercise testing is a very valuable aid in predicting and following cases of ischemic heart disease. The state of lipid peroxidation and antioxidants level could give a clue to the diagnosis of cases at risk, especially when combined with treadmill exercise testing, and may influence the prognosis and prevention of CAD.

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Proliferating cell nuclear antigen index and nm23 expression in osteosarcoma in relation to disease-free survival and tumor grade

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Osteosarcoma cases that have similar histological structure and same grade may have variable responses to the identical chemotherapy regimens, and show different prognosis. The current most common indicator of prognosis of an osteosarcoma patient is his response to neo-adjuvant chemotherapy. This is determined by measuring the amount of necrosis within the tumor mass following neo-adjuvant chemotherapy, which is a very difficult task.[1] Certain prognostic markers are needed for osteosarcoma patients. Both nm23 and proliferating cell nuclear antigen (PCNA) are the biologic markers those have been documented to have relationships with various tumors.[2-5] The nm23 is a tumor suppressor gene that is identified to be involved in tumor metastasis. There are many reports on nm23 expression in tumors; however, literary information is inadequate concerning nm23 expression and osteosarcoma together.[4] The PCNA, is a proliferation marker and can be detected by immunohistochemical methods in cells. It has been shown to relate with DNA polymerase delta sub-group and proliferation cannot occur in eucaryotic cells without it.[2,4,5] The purpose of this study was to investigate the PCNA and nm23 expression in osteosarcoma cells and their correlation with disease-free life period and tumor grade in search of new prognostic and predictive factors.

Formalin fixed and paraffin embedded tumor tissues of 51 patients were used in this study. Twenty-six of the cases (51%) were women, while 25 (49%) were men aged between 9-26 (median 16) years. Primary localizations were distal femur in 15, proximal tibia in 20, humerus in 11, proximal femur in 4, and radius in one patient. All patients' records were examined to determine the disease free survival. Specimens were confirmed as osteosarcoma and graded according to anaplasia, pleomorphism and nuclear hyperchromasia. Intravascular invasion for each specimen was also recorded **(Figure 1).** All patients were treated by neo-adjuvant chemotherapy, radical surgery, and adjuvant chemotherapy. Surgical treatments were amputations for 36, Enneking procedures for 11, resection arthroplasties for 3, and Van Nes procedure for one patient. The follow up period, free from metastasis or recurrence was defined for each patient as disease-free life

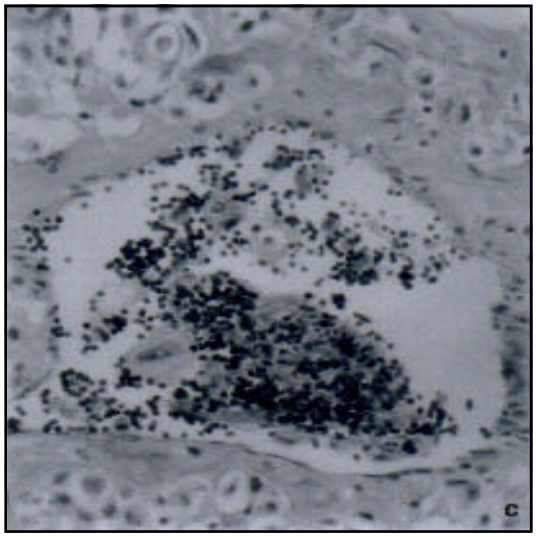

Figure 1 - Intravascular invasion of osteosarcoma (Hematoxylin and eosin x 115).

period. Six mm thick sections of each case were made on silicon coated slides from the original paraffin blocks. Immunohistochemical staining for nm23 was evaluated on both neoplastic and non-neoplastic tissues. For nm23 expression, the sections were incubated with polyclonal-sensitivity and specificity tested, primary anti-nm23 antibody, biotinylated anti-rabbit antiserum (Histostain-SP kit, Zymed lab. Inc., San Francisco, California, USA), and avidin dehydrogenase biotinylated horseradish peroxidase complex(Vectastain, Vector, Burlingame, California, USA). The polyclonal anti-nm23 antibody was cultivated against a synthetic oligopeptide recognizing the internal hydrophilic portion of the protein, which lies between bases corresponding to 354 and 404 of human nm23 cDNA (peptide 11). This antibody recognizes the products both from nm23-H1 and nm23-H2.[6] The nm23 immunoreactivity of the tumor tissue was graded as low and high according to the number of the stained cells and the intensity of the reaction by 2 independent observers. For PCNA determination, the sections were incubated with monoclonal PC10 epitaph carrying anti-PCNA antibody in IgG structure (DAKO, PC10, Glostrub, DENMARK), and a modification of the immunoglobulin enzyme bridge technique was applied using biotinylated horse anti-mouse antiserum (Vectastain, Vector, Burlingame, California, USA.) avidin dehydrogenase biotinylated horseradish peroxidase complex (Vectastain, Vector, Burlingame, California, USA). The PCNA index as the ratio of reactive to non-reactive tumor cells in a 40 x High Power Field (HPF) was measured for each slide in 10 different HPFs and the mean was accepted as the PCNA index of the specimen. Positive controls were used for each immunohistochemical study session of nm23 and PCNA. The Pearson correlation tests were used for analyzing the data. *P*-levels less than 0.05 were considered to be significant.

No recurrence was observed in any patients, but distant metastasis was present in 31 after a mean follow up period of 53 months. Twenty patients were disease free at the latest evaluation. Intravascular invasion was determined on 10 specimens out of 51. Thirty cases (58.8%) demonstrated high nm23 expression. There was no significant relationship between nm23 over-expression, and disease-free life period. Weak negative correlation was detected between tumor grade and high expression of nm23 (p=0.050, r= -0.27). Intravascular invasion rate, age, and gender were independent from nm23 over-expression. The PCNA index ranged between 10-90%. The median value was 40%. Those with less than 40% PCNA index (35 cases, Group 1) and those with PCNA index 40% and more (16 cases, 33.3%, Group 2). Disease free life period was significantly longer in Group 2 than Group 1 (p=0.008, r=0.366). No correlation was detected between PCNA index and tumor grade, age, gender, and intravascular invasion **(Table 1).**

Since the advent of modern chemotherapy, eventually leading to limb salvage surgery, the quality of life and outcome measures of osteosarcoma patients have demonstrated significant improvement. Unfortunately, there are still no certain prognostic markers for osteosarcoma patients other than histological response to neo-adjuvant chemotherapy. This is especially important, since these patients are mostly young individuals with a long life expectancy. New methods are needed to sub classify osteosarcomas relating to their prognosis and drug sensitivity.[1] The purposes of our study were to investigate the role of PCNA index and nm23 reactivity in osteosarcoma and try to find clues for new prognostic tools. The reasons for choosing these 2 biological markers were their previously documented relationship to prognosis, as well as their roles in proliferation and metastasis of tumor cells in some tumors.[2-5] In this study, although there was no correlation between nm23 positivity and disease free life period, nm23 reactivity seems to be low in low grade tumors. Disease free life survival found to be significantly longer in patients with higher PCNA positivity.

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Table 1 - Relationship between nm23, PCNA reactivity and clinicopathological features osteosarcomas.

Parameter	nm23		Significance	PCNA		Significance
	Low (%)	High (%)		<40 (%)	≥40 (%)	
Gender						
Female	12 (23.5)	14 (27.4)	ns	19 (37.2)	7 (13.7)	ns
Male	9 (17.6)	16 (31.3)	ns	16 (31.3)	9 (17.6)	ns
Age (years)	16.04 -	16.1 -	ns	15.9 -	16.4 -	ns
Grade						
Low	5 (9.8)	- -	*p*=0.05, r=-0.27	4 (7.8)	1 (1.9)	ns
High	21 (41.1)	25 (49)	*p*=0.05, r=-0.27	31 (60.7)	15 (29.4)	ns
DFS (months)	44.7 -	36.6 -	ns	29.5 -	62.7 -	*p*=0.008, r=-0.366
IVI						
(+)	15 (29.4)	26 (50.9)	ns	29 (56.8)	12 (23.5)	ns
(-)	6 (11.7)	4 (7.8)	ns	6 (11.7)	4 (7.8)	ns

DFS - disease free survival, IVI - intravascular invasion, PCNA - proliferating cell nuclear antigen, ns - not significant

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Medicolegal deaths in children and adolescents

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Accidents are the leading causes of death in all industrialized countries, and in a growing number of developing countries. Trauma is a major cause of death in children, especially those between 5-14 years. Fatal injuries are causing increasing concern from the age of one year up to adulthood. An analysis of the causes showed that most were preventable.[1,2] The situation in our country, and in our region, is not adequately known. In the present study, we describe the epidemiology of child and adolescent (0-18 years) mortality in Diyarbakir, Turkey over a recent 4-year period, and discuss both the leading causes of injury and available prevention measures.

We retrospectively reviewed all forensic cases referred to the Diyarbakir City forensic section, during the 4-year period 2000-2003. Of these, we analyzed all children and adolescent deaths and included victims younger than 19 years of age in our study. We considered the case file information from the autopsy reports and hospital reports for age, gender, origin, cause and manner of death, season, and the state of hospitalization before death.